ASSESSMENT OF ATTITUDES TOWARDS PARTICIPATION, WILLINGNESS TO PARTICIPATE, AND COMPETENCE TO PARTICIPATE IN RANDOMISED CONTROL TRIALS: A CROSS SECTIONAL QUALITATIVE AND QUANTITATIVE SURVEY OF PSYCHIATRIC PATIENTS AND KEY FAMILY MEMBERS USING THE "PROSPECTIVE PREFERENCE ASSESSMENT" METHOD AND THE MacARTHUR COMPETENCE ASSESSMENT TOOL FOR CLINICAL RESEARCH (MaCAT-CR)

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Dissertation submitted in partial fulfilment of the requirements of
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CERTIFICATE

Certified that the dissertation titled '**Assessment of attitudes towards participation, willingness to participate, and competence to participate in Randomised Control Trials: a cross sectional qualitative and quantitative survey of psychiatric patients and key family members using the "Prospective Preference Assessment" method and the Macarthur Competence Assessment Tool for Clinical Research (MaCAT-CR)'** is a bonafide record of original research work undertaken by Dr.Donae Elizabeth George, in partial fulfilment of the requirements for the award of the degree of Doctor of Medicine (MD) in Psychiatry.

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Certified that the dissertation titled '**Assessment of attitudes towards participation, willingness to participate, and competence to participate in Randomised Control Trials: a cross sectional qualitative and quantitative survey of psychiatric patients and key family members using the "Prospective Preference Assessment" method and the Macarthur Competence Assessment Tool for Clinical Research (MaCAT-CR)'** is a bonafide record of original research work undertaken by Dr.Donae Elizabeth George, in partial fulfilment of the requirements for the award of the degree of Doctor of Medicine (MD) in Psychiatry, under my guidance and supervision.

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DECLARATION

I declare that this dissertation is my own work and has not been submitted in any form for another degree or diploma at any university or other institution of higher education. Information derived from the published or unpublished work of others has been acknowledged in the text and a list of references given.

Vellore, **Dr. Donae Elizabeth George**

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CHAPTER

Abstract

TITLE OF THE ABSTRACT:

Assessment of attitudes towards participation, willingness to participate, and competence to participate in Randomized Controlled Trials: a cross-sectional qualitative and quantitative survey of psychiatric patients and key family members using the "Prospective Preference Assessment" method and the MacArthur Competence Assessment Tool for Clinical Research (MaCAT-CR).

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OBJECTIVES: To understand the perspectives of Indian patients undergoing treatment for major psychiatric disorders, and of their relatives, regarding participation in randomised clinical trials,and to assess their competence to consent**.**

METHODS:A cross-sectional quantitative and qualitative study using the "Prospective Preference Assessment" method on moderately-ill, consenting, psychiatric inpatients, and their relatives, assessed their attitudes to participation in randomised clinical trials (RCTs); their comprehension about information regarding two hypothetical trials; their willingness to participate; and the barriers and facilitators to participation. Clinical assessments of the capacity to consent were supplemented, in a sub-set, by independent assessments using the MacArthur Competence Assessment Tool for Clinical Research (MaCAT-CR). Quantitative data were presented as frequencies and qualitative data from audio-recorded, verbatim transcripts, were analysed for themes using the "Grounded Theory" framework.

RESULTS: All twenty participants (9 patients, 11 relatives) endorsed the need for RCTs and their methods; and altruism as a motive for participation. Only 50% were willing to participate in the hypothetical trials. Comprehension of information sheets was sub-optimal. Trust in doctors and organisations, and the opinions of family members' facilitated participation. Unfavourable risk/benefit ratios, the use of placebos, distrust in doctors and organisations, financial and other hardships, and opinions of family members were barriers. The majority of participants judged competent on clinical assessment failed formal tests of competence to consent.

INTRODUCTION

Randomized control trials (RCTs) are considered to provide the least biased method of evaluating the efficacy of drugs and other interventionsused in healthcare [1]. Well conducted RCTs form an integral part of the external research evidence that is meant to be summarised in systematic reviews and incorporated with clinical expertise, and the values and preferences of patients, in the endeavour called “Evidence-Based Medicine” [2]. For RCTs to produce valid and reliable results, their methods need to be robust in order to ensure that biases have been minimised, and that known and unknown confounders are balanced across treatment arms at the start of the trial [3, 4]. However, these methods used in RCTs that increase the reliability of their results differ from the components of clinical care that patients and their relatives expect from clinicians. This may give rise to ethical issues when vulnerable populations are enrolled in such trials without fully appreciating the potential risks involved, and the deviations in clinical trials from usual clinical practice.

Over the past decade, there has been an increase in the number of trials “out-sourced” to low and middle income countries, in order to ensure that adequate numbers of people are recruited, so that the required sample sizes are adequate for the purposes of scientifically valid analyses [5]. This shift in the settings where clinical trials are being conducted have been met with concern from some quarters about the need for such trials, and the potential for coercion and misinformation that may be used to recruit illiterate participants from low socio-economic backgrounds. They have also been welcomed by others due to the potential for financial benefits, and the improvements in knowledge and infra-structure that participation in such trial is associated with [6, 7].

In order to protect participants recruited to such trials, current International and Indian ethical guidance emphasises the importance of informed consent to ensure that patients and their care-givers participate in these trials after having understood the potential benefits, risks and procedures that participation entails; however, this consent needs to be voluntary, fully informed, and freely given [8-10]. Concerns have been raised about the quality of informed consent obtained in developing countries, and also of the validity of consent provided by psychiatric patients; and although evidence obtained from Indian patients regarding their views to participation is gradually emerging, this is insufficient to adequately inform the design and conduct of trials in Indian populations that meetethical standards, and yet also meet the requirements of scientific validity [5-7].

This pilot study was conducted in order to ascertain the views of psychiatric in-patients undergoing treatment at ageneral hospital psychiatric department, and of their key relatives, regarding their willingness to participate in clinical trials in general, and their willingness to participate in a hypothetical trial in particular. The barriers and facilitators to participation were also explored. Their comprehension of the information provided as part of the informed consent process, and their capacity to consent to participate were additionally investigated.

This study used a method called “Prospective Preference Assessment”that is aimed at improving recruitment for future trials, by simulating recruitment, thereby helping forecast enrolment rates, identifying problem areas, and illuminating differences between participants and non-participants [11, 12]. A cross-sectional framework and a mixture of quantitative and qualitative methodswere used in this study to explore the attitudes of psychiatrically ill patients and their relatives towards participation in clinical trials, and of this method of ascertainment of this information. Knowledge of

these attitudes and opinions will help in developing patient information materials catering to relevant and specific needs of Indian patients. Understanding the facilitators and barriers to participation in trials in this population will help in designing trials that are more patient-friendly and effective. Evaluating their comprehension of the information provided and assessing their capacity to provide valid informed consent will help in understanding the ways in which information should ideally be presented in order to be better understood; and will also inform those designing and conducting trials about the methods to be used to ensure that the consent given is valid, while ensuring that the methods important to ensure reliable results are also optimally utilised. Such insights into the mind-set of this vulnerable population can guide clinicians to plan better clinical trials in psychiatry that are both scientifically valid, and ethically defensible.

Objectives and Aims

The objectives of this cross-sectional, quantitative and qualitative study were to understand the perspectives of a sample of Indian patients undergoing treatment for major psychiatric disorders, and of their relatives, regarding participation in randomised clinical trials, in order to inform the design and conduct of future randomised clinical trials involving Indian participants, particularly those with psychiatric disorders.

The specific aims of this study were:

1. To explore the attitudes of psychiatrically ill patients and their relatives towards participation in RCTs in general; and about the specific components of the methods of RCTs that minimize the risk of bias and increase the reliability of their outcomes, in particular; by presenting them with information about a hypothetical RCT that they are invited to participate in.

2. To assess the comprehension of psychiatrically ill patients and their relatives regarding the information provided in informed consent forms that was provided to them during the process of informed consent towards participation in the hypothetical RCT, in order to understand the proportions of patients with psychiatric disorders, and their relatives, who are able to fully comprehend the information provided so that validity of the consent obtained could be assessed.

3. To assess the willingness of psychiatrically ill patients, and of their relatives to participate in the hypothetical RCT, and to understand their reasons for participation or non-participation; in order to identify the proportions who would be willing to

participate in future RCTs, and to understand the cultural and other barriers and facilitators to participation.

3. To assess the competence of the psychiatrically ill participants in this study,and their relatives, to provide valid consent to participate in research,based onclinical judgements obtained from standard psychiatric interviews; and to compare, in a subset of participants in this study, the correlation between the judgements of a trainee-psychiatrist and the independent assessment of competence obtained by an experienced consultant psychiatrist using the MacArthur Competence Assessment Tool for Clinical Research (MacCAT-CR).

Review of Literature

This section selectively reviews the existing international and Indian literature regarding the role of RCTs and other study designs in providing reliable evidence to inform healthcare decisions; the methods used in RCTs to ensure reliable results; and the ethical issues that arise due to the use of these methods, including the issue of "therapeutic misconception" that arises when patients seeking clinical care are involved in research. This section also briefly reviews the specific problems involved in including vulnerable populations in research, the empirical evidence from India and elsewhere regarding the attitudes of participants in clinical trials and their comprehension and capacity to consent to research. The methods used in such studies are also reviewed, as well as the instruments used in such research, in order to provide information relevant to the methods used in this study, and to clarify the results and interpretations from this study.

Generating reliable evidence for the effects of interventions: the importance of randomized controlled trials

Every question for which an answer is sought from research should ideally utilise a research design that is best suited to answer that particular question [3, 4]. Randomized Controlled Trials (RCTs) are considered the least-biased experimental design to evaluate the efficacy (and short-term safety) of interventions used in health care [1-4]. In the hierarchy of study designs that range from the designs most prone to bias to those least likely to introduce bias, RCTs (and systematic reviews of RCTs) are considered as the "Gold Standard" for evaluating the effects of interventions used in medicine and in healthcare [13]. Evidence for the efficacy of interventions derived from case series cannot provide reliable evidence since, in the absence of a control

group that did not receive the experimental intervention, one cannot be entirely sure that the differences in changes in clinical outcomes from baseline are due to the effects of the intervention alone [1-4]. Having a control group (consisting of no intervention, or a placebo intervention, or standard care, or another active intervention) helps to determine if any differences in outcomes between the experimental and control groups could be accounted for by chance (random variations), or as a result of spontaneous remission of the condition being treated, that is very likely in some conditions, such as psychiatric disorders [1-4, 14, 15].However, for the interpretation of the results of RCTS to be accurate, the participants in the experimental and control arms should be identical in all respects at the beginning of the trial in terms of confounders (demographic or illness variables that could independently result in better or worse outcomes other than that due to the experimental or control intervention) [3, 4, 14, 15].In an RCT, the process of randomisation creates groups that have similar prognoses at the outset; this is achieved by randomisation resulting in known and unknown confounders being balanced between the intervention arms, provided the sample size is reasonably large [3].

Observational studies (cohort studies and case-control studies) offer the best study design to answer questions regardingthe causation of diseases; and for detecting rare events, or of adverse events that may occur much later than the duration of the average RCT [1, 3, 16]. Observational study designs also offer an alternative to RCTs when RCTs are impractical, or are considered unethical [17]. However, observational evidence may beaffected by selection biases due to confounding [1-4, 13-15]. Reliance on observational data to inform decisions regarding interventions can be seriously misleading, and empirical evidence indicates that observational studies

generally tend to over-estimate the beneficial effects of interventions compared to RCTs, though the direction of benefit may not always favour the experimental arm; and is unpredictable [18, 19]. One example of the misleading effects that reliance on observational evidence can produce was the previous wide-spread recommendation of using hormone replacement (HRT) for prolonged periods in peri-menopausal and post-menopausal women to achieve better cardiovascular outcomes that was based on observational data;however, a systematic review of RCTs concluded that long-term HRT was associated not only with a higherrisk of developing adverse cardiovascular outcomes; there was also evidence for a higher risk of developing breast and colon cancer, and even dementia in older,previously healthy, women [20]. Even controlled clinical trials that are not randomized are not reliable in their estimates of effects due to the possibility of selection bias [19].

Key issues in RCTs that minimise the risk of bias and yield valid results

The various biases that can result in outcome estimates that deviate from the "truth" or yield wrong results that were demonstrated in empirical research are:

a. *Selection bias:* Selection bias refers to the imbalance in the experimental and control groups with regard to important prognostic variables at the start of the trial that result in outcome estimates that favour those with a better prognosis, rather than being due any of the interventions or control conditions [1-4]. Selection bias can be minimised by the process of randomisation, where each eligible participant has an equal chance of being allocated to the experimental or the control intervention and this can be best achieved if the process of creating the random sequence is done using methods used to generate a random sequence that can be concealed from those who recruit participants to the trial. In other words, the method used to generate the randomisation sequence should ensure that allocation

to intervention(s) or the control condition could not be predicted beforehand by the trial participant or the person recruiting participants. Therefore methods of randomisation such as using alternation, or days of the week, or any other method that cannot be concealed does not fulfil this requirement [3]. Methods to create a randomisation sequence that do fulfilthis requirement include simple techniques such as tossing a coin, drawing lots or referring to a table of random numbers, to more technologically-evolved methods such as using computer-based or online sources to generate the randomisation sequence. Concealing the randomisation sequence from those who recruit participants (called allocation concealment) can then be ensured so that the process of randomisation cannot be subverted by knowledge of the trial arm that the next participant would be allocated to. This can be achieved by using serially numbered, sealed, opaque envelopes containing the allocated treatment that is known only to the person generating the random sequence and that is opened only at the point of recruitment by a separate person who has no access to the randomisation code. Even more fool-proof methods are used such as central randomisation and allocation to intervention arms using inter-active voice response systems at a remote site, or by dispensing medications from pre-packed, serially numbered containers with the interventions controlled by the pharmacist that ensures that other investigators are unaware of which of the trial arms the participants would be allocated to. Randomisation therefore is a two-stage process wherein generation of the random sequence is followed by, or combined with, concealing the intended allocation till recruitment. The process of randomization (and concealment of allocation), if properly done will balance known and unknown confounders, such as age, sex, severity or duration of disease or lifestyle variations, and thereby minimize the likelihood of selection bias.

Empirical evidence demonstrates that trials that do not ensure allocation concealment of the random sequence are associated with over-estimates of treatment efficacy usually favouring the experimental intervention by as much as 38% [19].

b. *Performance bias:* This refers to bias introduced by knowledge of treatment allocation whereby additional treatments are given to one group and not to the other, or ways in which the groups are treated in different ways so that the outcome estimates are influenced by this differential treatment rather than due to the effects of the experimental or control treatments [1-4]. Preventing those providing treatments from knowing what treatment is being provided to participants can be achieved by "blinding" or "masking' the interventions by using identical tablets or capsules (whether they are placebos or active interventions), or the "double dummy" techniques, where each participant gets an active intervention and a dummy or placebo intervention, in order to prevent investigators and participants from knowing the nature of the allocated intervention.

c. *Detection bias:* This refers to bias introduced in assessing, or reporting, outcomes caused again by knowledge of the allocated intervention and influenced by the pre-conceived impressions by the person assessing outcomes, or the trial participants, about the efficacy and safety of the interventions. These impressions may affect the results of the trial and have also been shown to affect the estimates of efficacy and safety of trials in ways not actually due to the interventions being evaluated [19]. Blinding the participant and the outcome assessor to the allocated intervention, by ensure adequate allocation concealment and using "masking,' will ensure that detection bias is minimised; though this is more important for

subjectively reported outcomes such as depression or pain, rather than for objectively ascertained outcomes, such as death or an automated blood result [1-4].

d. *Attrition bias:* If those who drop out from the trial,from among those randomised, are not accounted for in the analyses, then false estimates of efficacy and safety may occur, especially if the reasons for dropping out are related to lack of efficacy of the allocated treatment or due to their adverse events. The importance of attrition bias in providing wrong or biased outcome estimates depends on the proportions of those dropping out, and particularly if there is a differential drop-out rate between the experimental and control arms [3]. Methods used in analyses that compare the results between those who complete the trial according to the trial protocol and those who were analysed according to the arm in which they were randomised, irrespective of whether they completed the trial (intention-to-treat), will help assess if attrition bias contributed to wrong estimates of efficacy or safety [1-4].

e. *Reporting biases:* This refers to the publication of the results of clinical trials, or the selective reporting of certain outcomes and not of other outcomes, or reporting the results in ways that were not intended in the trial protocol, that depend on whether the results were statically significant, and favoured the experimental intervention [1-4,21-24].

While many other issues in the design, conduct, and reporting of clinical trials can impact on the accuracy and the reliability of their effect estimates, the above biases have been demonstrated in empirical research as having the greatest impact on whether the results of the trial deviate substantially from the actual results (internal validity) [1-4,19]. This internal validity of the trial's results is determined by the

trial's design and methods. External validity refers to the generalizability of the results to other settings and populations and this depends on the similarities between the setting, populations, methods, and outcomes used in the trial and those where the intervention is to be used. Hence, if the exclusion criteria are too stringent, or if the comparisons or ways of evaluating outcomes differ from those used in clinical care, then the results of the trial may not be applicable to clinical situations that prevail in the real world.

Reporting scientific methods and ethical conduct in clinical trial publications

In order that RCTs are reported in standard ways that ensure that the methods used were scientifically valid, authors are expected by many journals to submit their manuscripts pertaining to clinical trials in accordance with the guidance in the Consolidated Standards for Reporting Trials (CONSORT Statement) that is available from the website of the CONSORT group (http://www.consort-statement.org/). The CONSORT'explanation and elaboration' documents, checklists and flowdiagram of the trial's recruitment and analysis plan, were developed using an evidence-based approach toimprove transparency of reporting of the methods used and the results of randomized controlled trials. The CONSORT statement was first published in 1996 [25], and revised in 2001 [26], and in 2010 [27]. Various extensions that cover the reporting of cluster randomised trials [28], equivalence and non-inferiority trials [29], herbal interventions [30], the reporting of harms [31], pragmatic trials [32], and abstracts of RCTs [33], have also been published. The 25 items in the revised CONSORT checklist weredesigned to help authors preparemanuscripts, and to help reviewers assess these manuscripts.One of the requirements of the *Uniform Requirements for Manuscripts Submitted to Biomedical Journals* (URMs) of the International Committee ofMedical Journal Editors (ICMJE) that are currently

endorsed by over 600 biomedical journals worldwide, is that reports of all RCTs conformto CONSORT. However, the qualityof reporting of methods in RCTs from low- and middle-income countries, including India, continues to suboptimal [34-37]. A recent editorial in the Indian Journal of Psychiatry requires authors of RCTs to now conform to the CONSORT statement while submitting manuscripts [38] and it is hoped that the transparency of reporting will improve, as it has done with some other journals [39, 40].

The ICMJE URMs also require that ethical standards endorsed in the Declaration of Helsinki [8] be reported in trial publications pertaining to approval by ethics committees and obtaining informed consent, as well as to the prospective registration of clinical trials before recruitment of the first participant.

Ethical issues associated with RCTs

There are many ethical issues that may conflict with the desire of researchers, clinicians, and society with regard to the conduct of RCTs. The most controversial issues concern 1) the use of placebos and 2) the validity of informed consent obtained from vulnerable populations.

The use of placebos in clinical trials

A major ethical issue about RCTs concerns the need for the trial. The foundation of any clinical trial is the "principle of essentiality" emphasized by the Indian Council of Medical Research in its research ethics guidelines [9]. RCTs are ethically justified only when there is genuine uncertainty (or equipoise) about the usefulness of two treatments for a specific condition [41]. The use of placebos, when standard treatments exist, has been the subject of controversy for many years, since participants are seemingly being denied an effective intervention. Proponents of the use of

placebos argue that, except in life threatening situations, where the use of placebos are not justified, the use of placebos helps to determine the extent of improvement attributable to the intervention rather than due to expectations of benefit or harm or due to chance or to spontaneous fluctuations in the condition [1, 4, 41]. Counter-arguments contend that any new intervention should be compared against standard treatment, since the use of placebos subject people to unethical harms caused by the continued disease process [6, 42].

Empirical evidence suggests that given the high placebo response rates in many psychiatric conditions (ranging from 15% to 50%, particularly in depression, and even in mania and to a lesser extent in schizophrenia), it may be misleading to make reliable conclusions of efficacy of a new intervention in the absence of a placebo comparator, even if compared with a supposedly effective treatments exist [4, 41]. In addition, psychiatric classification is based on a syndromic approach, driven by phenomenology and not informed by pharmaco-genetic or biophysical verification; blurred boundaries between disorder and distress result [41]. The interaction between the inexactness of the science and the fluctuating course of psychiatric disorders leads to a large proportion of patients in clinical practice and in trials experiencing a placebo effect [41].

Critics of placebo-controlled trials often confuse internal validity (the extent to which the methods of the trial enable reliable interpretations of the effects of the intervention) and external validity (the ability to generalize the findings of particular trials). Placebo-controlled trials provide opportunities for high internal validity but may be difficult to apply to clinical practice; trials without a placebo control may more easily mimic what clinicians wish to know about the efficacy of the new intervention compared to standard treatment, but may provide unreliable impressions

of efficacy. Both forms of (and methods to evaluate) validity are important. Alternatively, three-armed trials that include a placebo comparison and the standard intervention could address both forms of validity simultaneously [41].

Empirical evidence indicates that participation in RCTs is not associated with worse outcomes than for those who refuse participation [43]; and may even result in better outcomes (including for those in placebo arms), due to the better care given to people in trials [44]. The Declaration of Helsinki permits the use of placebo when no established treatment exists; and when it is proven beyond doubt that the placebo would not cause the subject harm or put him at risk of irreversible nature; and when it is absolutely essential to test the efficacy and safety of the intervention against a placebo purely for established scientific and methodological reasons [8, 45]. The position of interventions that serve as the gold standard in psychiatric care and research has also undergone considerable change over the years for both antidepressant and antipsychotic medication, thereby ensuring the need to constantly re-evaluate the relative benefits and harms of interventions that are considered standard care [41].

The US National Depressive and Manic-Depressive Association Consensus Statement on the use of placebos in clinical trials of mood disorders concluded that the placebo has a definite scientific role in mood disorder studies and that findings of equivalence between a new drug and standard treatment are not evidence of efficacy unless the new drug is also significantly more effective than placebo [46]. The situation is less clear in conditions such as schizophrenia where placebo responses are less dramatic than with depression, but do occur. The critical issue is whether the use of placebos has the potential to cause harm by deferring active treatment for the duration of the trial. There is no evidence to indicate that the short-term use of placebo does actually

cause harm, particularly if a) participants are closely monitored during the trial, b) are provided additional treatment to alleviate distressing symptoms, c) and are withdrawn after a reasonable time if they are not improved, or if they worsen, or experience adverse effects, or d) are permitted to withdraw consent due to any reason without any punitive consequences [47].

Issues related to informed consent and informed consent in vulnerable populations

The Helsinki Declaration states that in any research on human beings, each potential subject must be adequately informed about the aims, methods, anticipated benefits and risks the research may entail [8]. There have been many concerns that the process of obtaining informed consent for RCTs, particularly in psychiatry, and particularly from low and middle income countries, is inadequate. The concerns centre around, a) the way consent is obtained, where the process of securing valid consent is reduced to a single event exemplified by the signing of the consent form and b) the possibility that true, voluntary and informed consent has not been obtained, nor is possible, in people with psychiatric disorders [6, 42, 48, 49]. These is particularly important in situations where research is combined with care so that participants have trust in their care providers, and believe they will be getting standard and personalized care; while parts of the treatment actually address issues relevant to research such as the use of placebos, wash-out periods, randomization, and blinding [41]. This reduced appreciation of the risks of research participation and the over-estimation of the benefits is called the “therapeutic misconception” [50]. The Declaration of Helsinki specifically addresses this issue and recommends that dealing with this not uncommon phenomenon requires consent forms to clearly define, and the consent process to clearly articulate, what constitutes research and what constitutes care [8].

Empirical research indicates that older age, lower education, and worse health placed people at higher risk for holding a therapeutic misconception [50, 51].

Traditionally, people with mental illness are presumed to have poor decisional ability and this is borne out by empirical evidence [52]. However, systematic evaluation, even in non-psychiatric populations and in high-income countries, has shown that participants in randomized trials recall information poorly, are not often aware that placebos form one arm of treatment, demonstrate inadequate comprehension of the process of chance in treatment allocation, understand and use only a proportion of what is presented in consent forms, do not really understand the issue of equipoise, and participate not for altruistic reasons but because they expect some improvement by participation [53]. Cognitive dysfunction and the symptoms associated with impaired decisional capacity are not unique to schizophrenia and may occur with many other forms of illness [54]. Furthermore, studies have also shown that many people with schizophrenia are able to give informed consent and retain related information across time [54]. There is also evidence that individuals who have schizophrenia and lack adequate decision-making capacity may improve significantly with educational remediation [52-55].

The Declaration of Helsinki suggests that the individuals who are considered incompetent can be included in a research study provided it is proven that they are likely to benefit or even if they are unlikely to directly benefit then the intent of the said research is to promote the health of the population represented by the subject [8]. Also the research should entail only minimal risk and minimal discomfort to the vulnerable individual taking part in the study.

The Declaration also suggests proper justification of the research especially if it involves taking informed consent from people who are considered physically and mentally incompetent. The physical and mental condition of the subject should be the necessary characteristic that prevents such individuals from giving informed consent for research [8]. The Declaration also emphasizes that informed consent is not an all or none phenomenon; and that every effort should be made to gain consent from the individual or the legal representative to participate in and to remain in the research [8].

Thus, measures to protect vulnerable participants are needed to ensure that the methods of scientific research do not infringe on the rights of the mentally ill [56]. Adults who have psychiatric illness are often considered as requiring special consideration and protection as research participants. Institutional review boards often consider studies involving such persons using a different standard indicating that the concerns involving research with this population is different.

However, there is a range of capacity based vulnerability among people with psychiatric illness. There may also be a variation in this capacity within psychiatric disorders, and with improvement in psychiatric disorders with treatment, or worsening of symptoms and cognitive abilities due to progression of the disease [51]. For the advancement of the ethics of scientific research and in psychiatry itself, it is important to know the factors that regulate participation into clinical trials in this particular population.

Ethical principles and research in low income countries

The cardinal principles that govern and shape ethical research practices hinge on the upholding of respect for the autonomy of the individual, exemplified in adherence to

maintaining confidentiality, truth telling, informed consent, and protection of vulnerable people; and a belief in beneficence and non-malfeasance, where the benefits and safety of the individual take precedence over scientific, financial or monetary advantage [10]. The cornerstones of this belief are the careful risk-benefit assessment that precedes and continues after ethical review, and the process of informed consent that views participants in research as partners to be fully informed, rather than research subjects [10]. The principle of justice is manifest in a fair selection of subjects so that all people who might benefit from the fruits of research are included. Thus, from this ethical standpoint, people with psychiatric disorders should not automatically, by virtue of their diagnosis, be excluded from participation in research [8]. This principle is also evident in the order of preference in the selection of classes of subjects, where vulnerable people are excluded from being research participants if the research question can be answered by including less vulnerable people. Thus adults are selected before children, non-pregnant women before pregnant women and people with reduced capacity to consent or prisoners may be involved as research subjects, if at all, only on certain conditions [9, 10].

These principles have gradually eroded over the years in all cultures due to the fragmentation of healthcare and the pressures of academia and industry. In developing countries, cultural issues have compounded these challenges of the traditional ethical principles, where belief in the collective good has been given precedence over individual autonomy due the structure of paternalistic family systems and health care systems; with vestiges of the Guru-sishya (chela) model of interaction permeating the doctor-patient relationship; rather than the contractual model envisaged by the informed consent process [57]. Further subverting the process are the low bargaining power the average individual; inadequate advocacy support; inequities in access to

healthcare of any quality, the costs and distances involved in accessing healthcare, etc., so that what may seem reasonable compensation for participation in research may be powerful inducements to participate [41, 47]. Evaluating the views of research participants from low income countries and from different socioeconomic backgrounds is therefore crucial to our understanding of the barriers and facilitators to trial participation.

Assessing competence to consent in research

Informed consent is "consent given voluntarily by a competent individual who has received the necessary information, has adequately understood the information and after considering theinformation, has arrived at a decision without having been subjected to coercion, undue influence orinducement, or intimidation" [9].Informed consent is based on the principle that competent individuals are entitled to choose freely whether to participate in research or not andprotects the individual's freedom of choice, respect for the individual's autonomy, and protects the individual's rights [10].

Assessing competence to consent to participation is complex and often done arbitrarily. There have, therefore been calls by the US National Bioethics Advisory Commission for more formal assessments of the competence to consent to research among vulnerable subjects, particularly when research involves more than minimal risk; though this recommendation has also been criticized for requiring that all psychiatric patients be routinely evaluated formally for competence to consent to research, thereby presuming reduced capacity to participate in all people with psychiatric illness, unless otherwise proven [56].

Competence is a legal construct, and only a court can decide whether a person is competent or incompetent. Assessment of capacity is undertaken by medical and

mental health professionals, and while referring to competence, it is the clinical assessment of capacity, not the legal determinations of competence, this is assessed.

The capacity to understand and subsequently consent to research is particularly important for researchers, and this often raises problems since many people invited to participate inresearch have disorders affecting their cognitive and executive functioning. Specific populations like people with mental illness, AIDS patients, elderly persons with dementia and organic brain damage and people with substance use problems are ones whose capacity might be considered compromised; hence their informed consent process requires special focus. The US National Institute of Mental Health's Epidemiological Catchment Area study (ECA) estimated that around 3% of the adult population have severe cognitive impairments, rendering them incompetent and eligible to participate in research; even though they may agree to participate [56]. It is therefore important to develop and use standard ways of assessing the capacity to consent to participate in research.

Current standards [58] stipulate that assessment of competence (capacity to consent to research) should include evaluation of the person's ability to:

1. *Communicate choices*: This is an ability to maintain and communicate stable choices, long enough for them to be implemented;

2. *Understand relevant information*: Persons who cannot understand what they have been told about a treatment are not competent to decide whether to accept or reject it;

3. *Appreciate one's situation and the consequences*: Patients may comprehend certain information, but fail to grasp what it means for them.

4. *Manipulate information rationally*: This is the ability to use logical processes to compare the benefits and risks of various treatment options.

These aspects are often considered by experiences researchers in clinical assessments of competence to consent, but it is important that they be routinely applied in a standard manner to be sure that people with psychiatric or other vulnerabilities who may readily consent, and superficially appear to have the capacity to consent, are actually competent to consent.

The MacArthur Competence Assessment Tool for Clinical Research (MacCAT-CR) [59] is generally recognized as the best of currently available scales for formal assessmentof competence to provide valid informed consent to participate in research [51]. It isalso the most widely used in empirical research on consent capacity and adequate performance onthe MacCAT-CR was used in the CATIE trialas part of the criteria for independent consent [60]. It assesses competence on four subscales: 1) Understanding information, 2) appreciation of the significance of the information, 3) reasoning with the information, and 4) expressing a choice. Decisional capacity depends on the context and there is noparticular level of ability to determine adequate capacity in all circumstances [59]. Studies vary in level of risk and in the risk/benefit ratio. Total comprehension and appreciation along with high levels of reasoning abilities in patients with cognitive impairment might be considered unrealistic. An all or none phenomenon with rigid cut offs fails to take into account the possibility of different levels of competence that might be required depending on the nature of the project for which the consent is being sought. Thus what has been suggested is that instead of taking a fixed level of competence, a sliding scale would allow competence determinations to take in to account various factors which might influence a person's ability to comprehend, appreciate, reason and express his willingness to agree or

disagree to participate in a research project. General consensus exists thatas the degree of risk increases, a higher level of capacity is desirable. The MacCAT-CR has noestablished cut-score or algorithm for categorical determinations of capacity or incapacity; and it is recommended that the scores oncapacity assessment instruments, though helpful, should generally be supplemented with other important information, such as mental status and decision-making context [59]. The scores on the MacCAT-CR have not been validated in the Indian context.

Understanding trial participant's perceptions about participation in clinical trials and of the facilitators and barriers to participation

In recent years, the fraction of eligible patients who enrol in clinical trials has decreased worldwide [61]. This results in more time being required for completion of trials thus delaying important information and also in results being biased. Underpowered studies, at completion are unable to determine whether the treatment does more good than harm and hence raise ethical issues. Investigations of recruitment show that approximately only 50% of studies achieve their recruitment targets [62, 63]. One of the most important factors in the success of a trial is the willingness of the eligible participants to enrol into the trial. It is, therefore, important to explore and address the main factors affecting willingness to participate in trials. Understanding the barriers to participation can help to formulate interventions addressing those concerns. Identifying the factors facilitating trial participation can help in modifying trial designs to agree with participants' wishes, particularly if these wishes were ascertained in advance.

Attitudes towards participation in clinical trials

Attitudes of participants towards research in general have been studied across cultures and specific sub-populations. These studies indicate that clinical trials are viewed in general as being necessary and important, among participants and non-participants of these trials [61, 64-70]. Socio-demographic variables, psychological factors, monetary and health incentives were shown to affect willingness to participate in randomized controlled trial these studies. Although altruistic motives were given as the reason to participate, the decision to participate was also found to be associated with perceived health or monetary gains[69].

Other factors that have been discussed in literature include the patient therapist relationship and the perceived trust the patient has in the doctor and the organization. Trials done among ethnic minorities specifically indicate that a sense of obligation to the medical personnel involved in recruitment and a sense of mistrust were significant factors affecting the participation in trials [69, 70].

Barriers and facilitators to participation in clinical trials

An increasing number of studies have assessed barriers to participation in clinical trials; of these only the findings most relevant to this study are presented here. A meta-analysis of all studies evaluating the factors and barriers, from the perspective of potential Indian participants, contributing to their participation in clinical trials, identified through systematic searches of published literature, six qualitative studies and one survey that evaluated factors affecting the participation of Indian subjects [69]. The results showed that personal health benefits, altruism, trust in physicians, earning extra income from participation, detailed knowledge provided by the informed consent process and the methods used for motivating participants were the factors that increased participation; while mistrust of the organisation conducting the

trial, concerns about the efficacy and safety of trials, other psychological reasons, the burden posed by the methods used in the trial, fears about the confidentiality, issues related to dependency, and the use of language that was difficult to understand, were considered as barriers to participation [69]. In a quasi-experimental study involving vignettes presented to 1,277 Swiss patients, a higher willingness to participate was found when a new drug had no side effects, no additional visits were required, the information given balanced benefits and harms, the results were in the public domain, and the project was approved by a research ethics committee. In contrast in this study, destruction of blood samples at the end of the project, the use of placebo controls, and random allocation to study arms were associated with a lower likelihood of participation. Other variables such as funding sources, financial rewards, the need to complete a questionnaire, and the clinical need versus the potential economic purpose of the study did not influence willingness to participate [71]. In another study done on Indian patients attending a government tertiary care centre, 70% of 102 adults approached to participate in a 'mock trial' refused consent to participate [72]. More females than males refused participation. The reasons for refusing to participate included fear of giving more blood, reluctance to take a new drug, inability to make independent decisions, fear of tests, feeling too sick to participate, and not wanting to interrupt treatment [72]. Among those who agreed to participate, wanting to help the medical community, trust in their doctors to do only good, and wanting relief from pain were the most important reasons offered by participants [72]. The decision to participate was not influenced by the amount of information provided in the informed consent form [72]. This study highlighted two major aspects of recruitment to clinical trials in India. The first is that large numbers of patients may actually refuse to participate in clinical trials, but since this trial was not designed to test actual

recruitment and was conducted in a government hospital where costs were largely borne by the provider, it is unclear if access to care that is dependent on trial participation will change these estimates among those who cannot access routine clinical care due to financial constraints. Secondly, it highlighted that consent to participate may not be influenced by the amount of information provided in consent forms but by the other factors associated with participation such as the desire for personal benefit, altruism, and trust in their doctors. Thus, it may be that many patients who consent to participate in clinical trials do not actually understand the contents of consent forms adequately enough to provide what would be considered valid and informed consent. Since a placebo condition was not part of this study, it is unclear if Indian patients would subscribe to the use of placebos.

Consent forms are typically not be understood by average persons because they are too long, too complex, incomprehensible, and often written by lawyers than educators [53]. Conversation in securing informed consent is more reliable when the physician can assess the actual understanding of patients and evaluate their legitimate or irrational concerns. However, the information sheet and informed consent form are necessary in clinical research to ensure that the information provided was uniform and reasonably comprehensive.

Empirical research with psychiatric patients has demonstrated that patients are able to understand and use only a small proportion of information provided in consent forms, and this is especially true with depressed patients and those with schizophrenia [53, 73]. However, conflicting findings have emerged from Indian studies.

In a postal survey of 3622 physicians, several constraints in obtaining informing consent were noted, particularly concerning illiteracy of patients. In this survey, the

opinions on the amount of information to be provided to obtain informed consent revealed that informed consent procedures were far from ideal [74]. Structured interviews with a sample of subjects who were users of health care revealed that the majority was dissatisfied with many aspects of the physician- patient encounter including the amount of information provided [75]. Physicians interviewed felt more frequently than patients did that illiteracy was an impediment to obtaining informed consent. This study found that patients often felt that information about the nature of investigations and prognosis need not be routinely revealed [75].

A systematic study of informed consent for a drug trial showed that the majority of Indian patients showed adequate comprehension of issues involved and exercised a clear choice. The study stressed the need for all physicians to provide adequate information about research, though the form of presentation itself needs to be simplified [76].

In a study of 100 consecutive patients in a tertiary care hospital in India undergoing gastrointestinal surgery to test understanding and retention of information provided about the procedure, the majority of patients reported that they appreciated being given adequate information. While older, less educated and poorer patients performed worse than younger, educated patients, 70% recalled salient information regarding the procedure [77]. However, qualitative study of people who had undergone ECT and their relatives revealed that many patients felt the information provided was inadequate; some felt coerced into accepting treatment and though all relatives and some patients had signed the consent forms, many did not recall the information provided. This opinion was influenced by their mental state before treatment as those who were voluntary admissions were more likely to be satisfied with the consent than thos who were admitted involuntarily [78].

Very few Indian studies have assessed ways to improve the process of obtaining consent. A randomized controlled trial to assess whether participants in a community-based nutritional trial who received group counselling prior to administration of informed consent understood the key components of the study and the consent better than those who received individual counselling; based on the hypothesis that group counselling would foster discussion among potential participants and enhance their understanding of the informed consent. No differences were seen between the groups in terms of comprehension of key elements of informed consent and randomization, although all participants were aware of the details of the intervention and that they were involved in research. Many reported that one of the main reasons for their participation was better access to affordable healthcare that participation provided, compared to usual care [79].

The importance of family members in providing consent was highlighted in some Indian studies [72]. Family members in Indiatend to have a protective attitude towards their relatives and often do not wish for them to be provided too much information or information that is considered upsetting. In a study assessing the attitudes of depressed patients and their relatives towards informed consent for ECT, the overwhelming majority of the patients and their relatives wished to be given information about the ensuing treatment procedure, as well as illness details and prognosis, and felt they could understand the information if presented in a simplified and clear manner. The majority felt that their consent for treatment was necessary; however they wished that their doctors be the final decision-makers regarding the need for ECT. Psychotic symptoms and past exposure to ECT differentially affected these attitudes. These attitudes did not change significantly as a result of treatment. While patients' attitudes did not significantly differ from relatives' attitudes in

general, significantly more relatives felt information should be withheld from patients [80]. The last feature is a fairly common finding in clinical practice and suggests the need to involve relatives in treatment decision making as well as educating them on the need to divulge information to patients in the interests of ensuring treatment compliance [81].

Involving patients and relatives in designing research

It is widely accepted in many developing countries that involving service users in the design of research will result in more relevant researchquestions being developed, a higher level of trial recruitment and participation, better methods being used, better design of information to be provided to patients, and better interpretation of the findings from these studies [82, 83] . Most clinicians and researchers as well as trial participants welcomed this greater involvement [83]. However, it is unclear if Indian researchers and Indian trial participants would hold similar views given the paternalistic nature of the doctor-patient relationship traditionally seen in India.

Prospective ascertainment of the views of potential trail participants

Prospective preference assessment (PPA) was proposed as a method to increase participant recruitment in clinical trials by evaluating potential trial participants' motivations for participation, and their concerns about participation in a planned trial,before formal recruitmentin clinical trials [84].This method would also be able to identify those patients to whom a trial's results may be relevant, and would also protect the interests of participants [84]. The method involves presenting a hypothetical trial design and using both quantitative and qualitative measures to elicit willingness to participate in the trial along with the motivations and concerns participants have about trial participation [84-86]. Such interviews also include demographic and disease-specific data to investigate the ways in which people who express willingness to participate differ from those who do not.

This approach has other uses too, as it can be used to test and enhance understanding by potential participants of the key concepts of the trial(apart from the motivations and concerns regarding potential participation), and can also be used to evaluate

changes in understanding following educational interventions. Only 12(6.3%) of one hundred ninety patients with schizophrenia recruited in a study using this method were assessed to have understood all key trial-related concepts at baseline, though this proportion increased significantly after a brief educational intervention [85]. In this study, younger people and those with higher levels of education were significantly more likely to have better understanding of the prosed methods. Here too, the main reasons cited for wishing to participate in were personal medical benefits and altruistic desire to help others; while concerns regarding the safety of the trial medication were also expressed by the majority [85]. The PPA method was also used effectively in a vaccine trial to predict and improve enrolment rates [11], and to identify subgroups of potential participants who would need additional education to increase recruitment in order to ensure that participants in a trial of dialysis were more representative of those who are treated by dialysis in clinical care [86].

Since in India, family members are often central to decisions involving participation of patients in clinical research, the views of the key family member of participating patients could also be ascertained using the same methods.

Issues related to the methods of assessing barriers and facilitators and the prospective assessment method

The PPA method involves presenting a hypothetical trial design and using both quantitative and qualitative measures to elicit willingness to participate in the trial along with the motivations and concerns participants have about trial participation. Such interviews also include demographic and disease-specific data to investigate the ways in which people who express willingness to participate differ from those who do not.

Hypothetical designs may not actually predict actual recruitment to a trial, though the indications are that there is a correlation between expressed willingness to participate and eventual recruitment [11, 85, 86]. The quantitative part of such studies provide estimates of frequency of willingness and the factors that differ between those who consent and those who do not; but more important is the qualitative part of such approaches that provide in-evaluations of the concerns, barriers and facilitators to participation. Such qualitative approaches use in-depth interviews of individuals, using a semi-structured approach followed by open ended and probing questions, often recorded verbatim and the transcripts analysed using thematic analyses [87].

One of these methods used to analyse qualitative data is the "Grounded Theory" framework [88, 89]. Grounded theory is as an inductive method for qualitative analysis that generates theory from data. The central idea is that it is grounded in, and remains connected to, the data, and in the understanding and experiences that people have about a phenomenon [88, 89]. An inductive method is one where the theory emerges from the data, in contrast to deductive theory, where the researcher starts with an abstract idea or theory and then tests propositions related to the theory. The greatest strength of grounded theory is that it goes beyond mere description and provides a method of developing an explanatory model that accounts for change and variation in human behaviour [88, 89].

Qualitative research also needs to follow reporting standards as much as RCTs are expected to follow the CONSORT statement. While no universally approved reporting standard exists for qualitative research, one such standard is the Consolidated Criteria for Reporting Qualitative Research (COREQ) [90].

Materials and Methods

Study design

This cross-sectional study used quantitative and qualitative methods to evaluate the attitudes of participants (patients and relatives separately) towards participation in clinical trials and their willingness to participate in a hypothetical trial and an extension of this hypothetical trial.

A quantitative survey using a semi-structured questionnaire assessed their attitudes towards participation in research based on the information provided in an information sheet inviting them to participate in this study that also explained the rationale and the methods of RCTs and the information sheets of the hypothetical trial. Qualitative methods were used to evaluate recorded and transcribed verbatim responses, clarifications and concerns to this information, and to evaluate their comprehension of the information sheets for the hypothetical RCT and an extension; as well as to evaluate the reasons they advanced as factors that might increase or decrease their chances of participation. The data were also analysed using quantitative and qualitative methods.

Setting

The study was conducted at the department of psychiatry, of a teaching general hospital in South India. The department has four units in all, with two units catering to adult psychiatry cases, one unit concerned with rehabilitative psychiatry and one unit catering to child and adolescent psychiatry. The in-patient services of the department are geared towards family involvement in care and include a 120 bedded hospital where patients stay with their family members for treatment for a variable

period of time; the average period being four to six weeks. The department caters to a variety of problems ranging from psychosis, neurosis, alcohol and substance related problems, mood disorders to adjustment, personality and relationship problems.

In-patient accommodation is of three types, depending on the socioeconomic status and financial resources of patients. The 'Annexe" provides dormitoriesfor four to six patients each and their attending relatives. The charges are nominal and concessional or free care is granted by the treating team for economically disadvantaged people admitted here. There are 20 beds in this category for adult patients. Single family units consisting of a room with a semi-detached toilet and kitchen that offer more privacy and space are available in the 'Low-cost private wards' for paying patients. There are 37 beds in this category for adult patients. The 'Private' ward consists of 18 single rooms (air-conditioned and non-air-conditioned) for adult patients, that are self-contained units consisting of a bed-room with an attached enclosed courtyard, dining space, bathroom, and kitchen.

The department is part of a teaching general hospital but is situated in part of the residential campus of the institution, and does not have a closed ward, though disturbed patients may be restrained in an open high-dependency ward with relatives in attendance and 24-hour nursing cover and doctors on call, and when less disturbed may be shifted to one of 12 'Acute care rooms'. Involuntary patients are admitted under the provisions of the Mental Health Act of 1987 [91].

All in-patients (and out-patients) are worked up by post-graduate registrars who discuss cases with consultant psychiatrists, or are worked up directly by consultants. In-patients are provided care by their allocated treating doctors, and a multidisciplinary team of psychiatrists, nurses, occupational therapists, and social

workers, and the emphasis is on humane and collaborative treatment, using an eclectic mixture of psychotherapy, education, support, occupational therapy, and medication. The primary therapist and the supervising consultant invariably develop a good rapport with the patient and relatives in view of the multiple sessions and time spent in clarification of diagnosis and discussion of management strategies that include pharmacological and non-pharmacological therapies.

Setting for data collection for the study

One of the assessment rooms in the hospital was chosen for conducting the interviews. Data collection was done in this room taking care to ensure it was quiet with minimal intrusions, and shielded from noise to ensure good audio-quality of the recorded interviews.

The patient and relative were initially met in the ward and if they agreed to participate, or required further information, they were later invited the interview room for the interviews. During the initial session, which was focussed on rapport building, both patient and the key relative were seen together, and subsequently they were interviewed separately. Non-participants were not present during the interviews.

The interviews for each participant were conducted in multiple sessions over many days as per the convenience of the participants. As the inpatient treatment programme includes occupational therapy and psychotherapy sessions with the individual therapists, care was taken not to interrupt their schedules as far as possible. The session for rapport building was not timed or recorded. It was understood from the pilot study that a good rapport was crucial for improving the quality of the interviews and hence these sessions were held prior to the starting of the interviews on separate days. The participants were informed regarding the credentials of the interviewers and

it was mentioned that the study was being done as a part of the training for the primary investigator's degree in psychiatry.

Participants

Participants were recruited from the adult units of the inpatient services of the department from July 2012 to October 2012. All patients admitted into the wards, satisfying the inclusion and exclusion criteria were eligible to become participants.

Inclusion criteria

1. Adult patients (18-65 years) admitted to the hospital for at least one week who consented to participate in this study with:

    a. A clinical diagnosis of ICD- 10 Major Depressive Disorder-single episode or Recurrent Depressive disorder (with or without psychotic symptoms), Bipolar Affective Disorder (with or without psychotic symptoms), Manic Episode, Schizophrenia, Schizo-affective Disorder, Obsessive Compulsive Disorder, Generalized or Situational Anxiety Disorders, Phobic Disorders, Somatoform disorders

    b. Clinical Global Impression Severity [92] score of 4 (moderately ill) or more

2. One key relative/care-giver, identified by a consenting patient with psychiatric illness, who provides informed consent to participate.
3. Language of communication is Tamil or English

Exclusion criteria

1. ICD 10 diagnosis of Substance use disorder, or Organic disorder, or Disorder due to brain damage or dysfunction, primary diagnosis of Personality Disorder, Adjustment Disorder
2. Acutely ill patients
    a. Requiring admission into the acute care rooms
    b. Who would require periodic monitoring in the acute care room in view of risk of harm to self or others
3. Patients and /or relatives who do not consent
4. Patient considered by treating psychiatrist as not suitable for participation in this study for any reason
5. Key relatives clinically diagnosed to have a current psychiatric disorder with clinical active symptoms of any degree of severity

Sampling methods

Consecutive inpatients were planned to be approached, but purposive and theory-based sampling was also employed to obtain adequate representativeness of the sample by ensuring that at least half the patients have a psychotic condition and the remainder a non-psychotic condition. This also helped to ensure that female patients, and those with lower levels of literacy, were also adequately represented.

Method of approach

A face-to-face method was employed taking time to develop rapport while informing potential participants of the study and inviting their participation while giving them

the informed consent form for the study. Following the rapport building session the interviews were recorded on a voice recorder after getting consent for participation.

Sample size

Thirty in patients and their relatives were planned to be recruited yielding a total sample of 60 participants. Since this is an exploratory study with in-depth analysis of attitudes and views, formal sample size determinations were not done. The intention was not for the sample to be representative of participants' views across India, but rather to achieve a saturation point of ideas and views.

Preparation of study materials

1. The information sheet regarding the nature of the study and the issues related to the methods used in RCTs were prepared in order to adequately inform participants of the details of the study and to aid their comprehension; and this information included the following elements:
    A. An invitation to participate in a study approved by the Institutional Review Board of the Institution and the purpose of the study;
    B. A statement that taking part in this study does not form any part of the treatment being provided at this hospital, and the decision to take part or not take part in this study will not affect the treatment provided at this hospital.
    C. The nature of research used to study new medicines and the issues related to the methods of RCTs that are aimed at minimising bias and confounders and the ethical issues these methods entail;
    D. Information about what they would have to do if they decided to participate, including the a) fact that they would be invited to provide responses to questions about their opinions about the nature of RCTs; b) they would be

invited to participate in an imaginary trial (and an extension), for which they would be provided details in an information sheet in the language of their preference (English or Tamil) and have this form explained to them, if needed; c) their comprehension of the details in the information sheet would be assessed; d) their responses during the interview would be recorded for transcription and analyses; e) an independent interview would be conducted within 48 hours or at the earliest by a consultant psychiatrist to assess their capacity to consent.

E. A statement of the extent of their responsibilities;
F. The potential benefits of participation;
G. The voluntary nature of their participation, and the possibility of withdrawal without any adverse consequences even after consent is given;
H. Financial disclosures about funding for this study;
I. Details about confidentiality and disclosure of the results of the study
J. Contact information of investigators.

The information sheet and informed consent forms were pilot tested and revised and the final version is provided in *Appendix 1a.* These forms were translated into Tamil and back-translated into English to ensure the accuracy of the translation; and the Tamil version is also provided in *Appendix 1b.*

2. Demographic data and illness details: Details of socio-economic status, and of the illness and included the following:

a. Socio-demographic (patients and key relatives):

- Age

- Sex
- Socioeconomic status as decided by the room category during admission
- Educational status
- Literacy level
- Occupation
- Relationship to patient/key relative

b. Clinical variables (for patients):

- ICD 10 diagnosis
- Duration of illness
- Duration of current episode/exacerbation
- Presence of active psychotic symptoms (Delusions/hallucinations) in the past 24 hours: Present/Probable/Unclear/Absent
- Current medication (antidepressant and dose/ antipsychotic and dose/anxiolytic and dose/ anticholinergic and dose/ mood stabiliser and dose/ other medication and dose
- Presence of treatment non-response in past
- Nature of the consent given for admission into hospital (voluntary/involuntary)
- Scoring on the Clinical Global Impression scale- severity

- Clinical assessment of grades of insight

c. Clinical variables (for key relatives):

- History of psychiatric illness and details
- Current evidence of psychiatric illness on clinical interview
- Any current medication

The data collection form used is provided in *Appendix 2*.

3. *The attitudes to research questionnaire:* This questionnaire was prepared based on the findings of the literature review and from clinical experience with Indian subjects and consisted of 20 questions with responses scored on a Likert-type scale ranging from Strongly agree/ Agree/ Do not know/ Disagree/ Strongly disagree and included the responses of Did not understand/ Other response. The 20 questions covered ten major themes. They were:
   a) The necessity of RCTs as perceived by the participants (question 1)
   b) The reasons for participation in RCTs (questions, 2, 4, 6, 11),
   c) Doctors motives in conducting RCTs (questions 3, 5, 7),
   d) Problems faced by patients in RCTs (questions 8, 12),
   e) Disadvantages of RCTs (questions 9, 10, 14),
   f) Opinions regarding the key elements of RCTs (randomization, blinding, informed consent) (questions 15, 16, 17),
   g) Involving patients in designing trials (question 18),
   h) Participation in trials as a duty of every individual (question 19),
   i) Willingness to participate in placebo controlled trials (question 20),
   j) Decision to participate as a family decision (question 13).

This questionnaire is provided in *Appendix 3.*

4. The information regarding the hypothetical trial was designed to contain the following elements, in addition to essential elements of informed consent stipulated in the ICMR ethical guidelines [9]:
    A. An invitation to participate in an imaginary trial and the purpose of this exercise
    B. A wash out period from existing medications if they decided to participate,
    C. A new study medicine that will be compared to a dummy medicine;
    D. The supposed effects of the new medicine on stress-related symptoms, and the possible adverse effects;
    E. The fact that participants will be randomised to either the new medicine or to placebo;
    F. The reasons for the randomised design;
    G. The fact that neither participants or investigators will be able to know what treatment was being provided due to the blinding and allocation concealment, and the need for this;
    H. The 8-week duration of the trial and the weekly assessments of symptoms and adverse events
    I. The need to be hospitalised for the first four weeks at least;
    J. The fact that trial medicines would be provided free and costs of treating any adverse events would also be free;
    K. The fact that sedatives and any other treatment needed for symptom relief would be provided;
    L. The amount of reimbursement for study related visits
    M. Details about confidentiality

N. Information about post-trial access to medicines and further treatment

These information sheets and informed consent forms were also pilot tested, translated into Tamil, back-translated into English and is provided in *Appendix 4a.*

5. *Assessment of comprehension regarding information provided for the hypothetical trial comparing a new drug versus placebo.* A questionnaire providing 10 statements to be answered True / False / Unsure / Do not know was prepared to test the information provided and included assessments about their understanding regarding randomisation, blinding, placebos, compensation etc, that would be used in the trial. This comprehension assessment questionnaire is provided in *Appendix 4b.*
6. *Qualitative interviews regarding the hypothetical trial:* During the audio-recorded interview, participants were asked if they would be willing to participate in the hypothetical trial and the reasons for participation or for declining to participate. A set of probe questions that were to be used to facilitate this interview were designed to ensure that participants freely expressed their opinions; and these questions are provided in *Appendix 4c.*.
7. *Information sheet regarding the extension to the hypothetical trial.* Participants were also asked to participate in an extension to the hypothetical RCT. The information sheet for this extension included information about the hypothetical trial but included additional elements designed to add to study burdens, and included blood tests, an ECG and an EEG. No wash-out period was used in this extension. The information sheet for this extension was also pilot-tested and revised; translated to Tamil and back-translated to English. The information sheet and informed consent form for this extension are provided in *Appendix 4d.*

8. *Assessment of comprehension about information regarding the extension trial.* Five questions scored as in the previous questionnaire assessing comprehension were designed to assess the comprehension of the information about the extension. These questions are provided in *Appendix 4e.*
9. *Qualitative interviews regarding the extension to the hypothetical trial.* The open ended questions designed to probe participants responses during audio-recorded interviews regarding their willingness to participate in the extension trial are provided in *Appendix 4f.*
10. *Assessments of competence (capacity) to provide valid consent to participate:* The primary assessment of capacity to consent was done during clinical interviews and included assessments of mental state, degree of cooperation, ability to comprehend the information provided and an overall assessment during the course of the interview about how decisionally-impaired, psychotic, or lacking in insight participants were. A sub-set of participants were independently interviewed using the MaCAT-CR that was adapted to assess the information provided in the information sheets and additional probe questions added. The MaCAT-CR used for this study is provided in *Appendix 5.*

Ethical issues

All participants were informed about the voluntary nature of their participation and their right to decline. The methods, information sheets used, and the full protocol of the study were approved by the Institutional Review Board (Research and Ethics Committees) of the Christian Medical College, Vellore. Data are presented to maintain the anonymity of the individual participants. Quotations used in the reports do not include any information that can possibly identify the participant.

Study conduct and Data collection

Step 1:

Patients admitted to the hospital, meeting the inclusion and exclusion criteria were enrolled into the study after obtaining their written, informed consent. The information sheet and consent form for participation in the study is provided in ***Appendix 1a and 1b***.Consent was sought for the interviews, for audio-recordings of the same, and for the assessment of competence using the MacCAT-CR.

Step 2:

Demographic and clinical data was collected in to a data extraction sheet. Information was obtained from the primary therapist, medical records and the patients for the same. The data collection sheet is provided in ***Appendix 2***. This time was also used to build rapport with the patient and the key relative.

Step 3:

All patients were assessed for severity of illness using the Clinical Global Impression (CGI) [92]. The CGI scale is a brief assessment tool in psychiatry comprising three items measuring illness severity, global improvement and therapeutic response. Each component is rated separately and the instrument does not yield a global score. For this study participating patients were rated only on the Clinical Global Impression scale Severity item, which asks the clinician the question of how mentally ill the patient is at the time of assessment, rated on a seven point scale:

1=normal, not at all ill

2=borderline mentally ill

3=mildly ill

4=moderately ill

5=markedly ill

6=severely ill

7=among the most extremely ill patients.

The rating is based upon observed and reported symptoms, behavior, and function in the seven days prior to assessment. For the purposes of the study this assessment was made for the preceding 24 hour period.

Step 4:

A clinical assessment of competence to provide consent of patients and their key relatives was made by the primary investigator before and after the completion of the interviews. Patients, who were assessed as not competent, were approached on two separate occasions at weekly intervals to re-assess competence. One key relative was recruited at the initial assessment for the attitudes to research questionnaire, if consent was obtained. The MacCAT-CR was administered to both members at the final assessment point.

Step 5:

Administration of the attitudes to participation in clinical trials questionnaire: This structured questionnaire was given to literate participants to read and was read out loud to non-literate participants. Responses were recorded by the research clinician, after verifying comprehension. This questionnaire assessed the attitudes of participants toward research participation in general and to the specific components of the methods used in RCTs ***(Appendix 3).***

Step 6:

Invitation to participate in a hypothetical RCT: The information sheet for the hypothetical RCT (***Appendix 4a***) was administered to participants as in step 5. Opportunities were provided to seek clarification regarding the contents of this information sheet and the clarifications requested were noted (and audio-recorded).

Step 7:

Administration of the questionnaire assessing comprehension of the information administered in the information sheet of the hypothetical RCT (***Appendix 4b)*** and the proportion expressing willingness to consent was noted. The key-relative's willingness for the patient to participate was assessed. Reasons for consenting or declining were explored using open ended questions and probes and participants were facilitated to express their opinions and concerns***(Appendix 4c)***.

Step 8:

Those who consented and those who refused to participate in the hypothetical trial were presented, an additional extension of the trial ***(Appendix 4d)*** that posed differences in interventions and increasing levels of inconvenience. The actions described in Step 7 were repeated for this extension as for the main hypothetical trial, assessing comprehension ***(Appendix 4e)*** using open-ended questions and clarifying probes ***(Appendix 4f).***

Step 9:

The MacCAT-CR ***(Appendix 5)***was administered on a separate occasion within 48 hours of the initial evaluation after re-affirming consent obtained earlier by the primary investigator. The assessments were performed and scored by the co-investigator (a consultant psychiatrist) using the standard procedures described in the manual accompanying the tool.

All the above assessments were audio-recorded (with the consent of participants) and transcripts were independently reviewed by the co-guide and guide.

Data handling and analyses

Quantitative variables

Socio-demographic and illness variables were summarised using frequencies and their distributions (if possible). The frequencies and nature of responses to the attitudes to research in general and the specific components of RCTs were calculated in patients and relatives. The proportion of participants who demonstrated adequate comprehension of the information for the hypothetical RCT was assessed. The proportions of participants that expressed willingness to participate and that refused participation in the hypothetical RCTs were determined.The proportion of participants who endorsed favourable views to RCTs and who also express willingness to participate in the hypothetical trials was assessed.

The proportion of participants considered to have adequate capacity on clinical assessment was further evaluated to evaluate the proportion assessed as adequate on the MacCAT-CR; on all the domains (Understanding information, appreciation of the significance of the information, reasoning with the information, and expressing a choice).The performance of participants' competence was evaluated using stringent standards (adequate on all domains); intermediate standards (adequate on three domains: Understanding information, appreciation of the significance of the information, reasoning with the information) and the least stringent criteria (Understanding information). The proportion of participants considered to have adequate capacity were also evaluated using scores that were 50% of the maximum possible for the above criteria.

Formal statistical analyses of differences in responses in relatives and patients and correlations planned were not possible due to the limited sample size.

Qualitative data and analyses

Data analysis on the transcripts of the audio-recordings of the interviews were undertaken inductively and iteratively based on the principles of Grounded Theory. The transcripts of interviews were checked for accuracy and were read by the investigators to identify commonly expressed themes and sub-themes. Based on this emerging themes and sub-themes a study framework was developed, where themes are coded because of their characteristics as being explicit, strongly held, reflective of good research ethics and for highlighting participant's concernsand increasing their comfort with trial participation. Illustrative quotations were selected for emerging themes and findings and were presented without being linked to participants in order to preserve confidentiality.

Results

A sample of 30 patients and relatives were planned to be recruited. However due to time constraints, and lack of sufficient patients who fulfilled all eligibility criteria, the sample size planned could not be attained.

During the period of the study, 20 patients and their relatives (40 eligible participants) were found eligible to participate according to the inclusion and exclusion criteria. Of these, eight patients and relatives (16) refused to participate in the study.

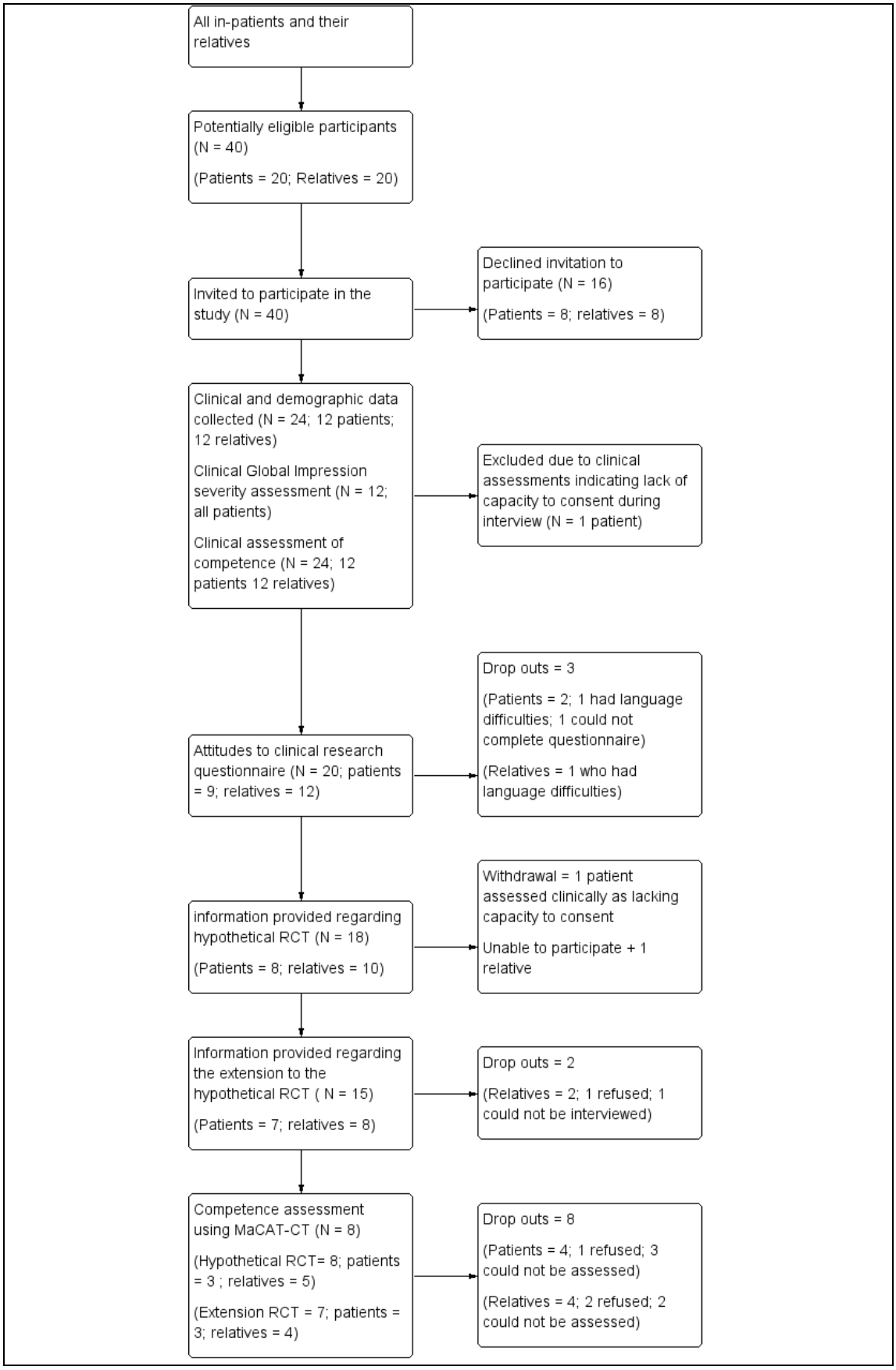
Of the 12 patients and their relatives (24 participants) who initially consented, three patients refused to give consent.

The reasons for refusal to participate were sought from all three. A voice recording of the interview exploring the reasons for refusal could be obtainedonly for one patient. The details regarding refusal were recorded as part of field notes for the other two participants. One patient and relative had given consent but was unable to attend interviews due to inconveniences and practical difficulties in coming for the sessions.

Figure 1 describes the flow of participants into the various components of this study.

Of the 24 participants who consented, not all completed all steps of the study as some refused to continue to participate at various time points or could not find time amidst their treatment schedules to complete assessments. One patient was assessed as not competent to provide informed consent during clinical assessments during the first interview; another patient was found to have clinically worsened during a subsequent interview and was declared as lacking capacity to consent and hence was withdrawn from the study

Figure 1: Flow diagram of participants recruited and who completed assessments



Socio-demographic details and illness details (of patients)

Of the 20 patients who were eligible to participate (Figure 1), 10 patients were voluntary admissions, while the other 10 were admitted at the request of their relatives under the provisions of the Mental Health Act. Sixof the patients were admitted in the private wards, 10 were admitted in the low cost private wards and four were admitted in the annexe dormitories. The mean age of the participants was 28 years (SD 8 years; range 18 to 47 years). There were equal numbers of males (10) and females (10) among the eligible participants.

Of the 12 patients who consented to participate (6 voluntary admissions), seven were females. Four were admitted in the private wards, five in the low cost private wards, and three in the annexe dormitories. Their mean age (SD) was 25 (6) years and their age ranged from 18 years to 38 years. Six of the 12 consenting patients (50%) and 6 of the 8 non-consenting patients (75%) were graduates, while five of the consenting patients (41%) and 1 (13%) of the non-consenting patients had a primary or secondary school education, and one in each group were diploma holders. Six of the 12 (50%) consenting patients had a CGI severity score indicating a moderate level of severity while the others were markedly ill; five (63%) of the non-consenting patients were moderately ill, two (25%) were markedly ill, and one (12%) was severely ill.

Five of the 12 consenting relatives were male (three were fathers of patients, one a grandfather, and one a husband). The seven female relatives were mothers of consenting patients. Six were graduates, five had some years of schooling (primary school = 3, secondary school = 2) and one was a diploma holder. Four of the consenting patients and relatives read and spoke only Tamil. Seven of the patients had a diagnosis (ICD 10) of schizophrenia, one had a delusional disorder, one had hypomania, one had mania without psychotic symptoms, Three of the 12 patients had very poor insight and two of them were subsequently deemed as lacking the capacity

to consent due to worsening of psychotic symptoms, two had recurrent depressive disorder (one with psychotic symptoms), and one had a dissociative motor disorder.

Attitudes to clinical research

The results of the 20-item questionnaire assessing the attitudes of patients (N = 8) and relatives (N = 10) towards participation in clinical trials are shown in ***Table 1***, grouped under the 9 themes and sub-themes. The quantitative results were supplemented by qualitative responses obtained by participants during interviews.

All the patients and relatives agreed that it was necessary to test new drugs scientifically before using them in clinical practice (Table 1). For example, one participant stated, ""I agree strongly regarding the clinical tests on patients. Without strong studies, it cannot be used in general manner." However, this general endorsement need not necessarily imply that all would endorse participation in clinical trials. One relative stated, "What I perceived is that it is simply a theoretical study and we want to talk about these things, but actually I do not intend my patient to be given any new medication even if it is dummy ones."

Regarding reasons why patients participate in clinical trials, all patients and participants felt that for patients, faith in the doctor and the institution are the most important motivating factors behind deciding to take part in a clinical trial. Altruism as a motive for participation was expressed by all the relatives and 75% of patients who felt that patients participate in research to help in reducing human suffering as a whole. However, half the patients agreed with the statement that patients participate in research trials because they expect to get personal health care and health benefits, while half the relatives disagreed with this notion. More than a third of relatives and more than half the patients disagreed with the statement that patients participate in research trials mainly because they expect to get monetary benefits.

Qualitative responses added other views for why patients may wish to participate in clinical trials. One person felt that participation depends on the type of medication being tested, "..It also depends on the intensity or like what type of medicine and what are the risks involved in that, so if it is a normal medicine like suppose paracetamol, maybe someone wants to try something similar to it, maybe nobody will object to it because that will not cause harm, but if it is such a medicine, which can harm in some other way then a patient can resist,….He will be a little hesitant."

Some felt that lack of response to other medication may be a reason to join a trial:"Certain patients may like to participate because they do not have any other options. Many tabs have already been experimented on him (patient). It has not been beneficial to him then he does not have any option, then let us try new medicine… that may be the one of the reasons"

"if there is no other medicines left for them, like suppose there is a such patient where there is no other medicine left for them, so maybe doctors want to try a new medicine, so it will be helping her or maybe he can take a risk whether this medicine can be helpful or harmful. so in that way it may be helpful."

Regarding monetary benefits one person felt it was morally incorrect to expect monetary benefits for participation in research, "..now we are staying here as a patient. You are asking our help for the research study. It is wrong to ask you to provide money for answering the questions which you asked…" Another stated, "If he is you know economically not strong, so for that for the monetary benefit he may try. Otherwise for the money no one will try to take a new medicine, maybe due to some circumstances…."

"Considering the risks in healthcare in new trials, healthcare cannot be compromised for monetary gains.."

Regarding trust in doctors and the organization doing trials, one person mentioned with regard to his experience with treatment of his relative, “I do not blame them (doctors). They tried to enthuse confidence in me at that time, but I could not believe them at that time. I did not have that much confidence at that time. Even if I believed them, I wanted to have a third opinion….”.The same person also mentioned that the asking of consent raises fear, “No body asked for my consent while going for aripiprazole,… but while going for the clozapine therapy everybody is asking for my consent, why my consent, why they are not starting it, so they are asking for the consent itself raised a lot of fear, no doubt, fear in myself particularly regarding granulocytosis….(side effects)”

Regarding the motives of doctors in conducting clinical trials, all the patients and more than three-quarters of the relatives felt that doctors do research trials with the sole aim of helping their patients.One participant stated, “They can find the medicine by doing a lot of tests as early as possible so that even the child in the mother’s womb can be prevented from this (illness). So we can do something for this. Thus, I cannot say that the doctors are doing for the fame or pride. They are also doing the service that we are seeing by our own eyes….”However, additional motives such as conducting experiments and promoting their careers were also endorsed by the majority of patients and relatives. One person disagreed that doctors do trials to help their own patients. He felt that the benefits would take time and so immediate results would not be got.

“… the research is not going to have any immediate result. Only if it is beneficial, he will have to go a long distance to establish it. Only after that the medicine can be generalized or approval to use the medicine in general can be given.”

Table 1: Attitudes to participation in clinical trials: responses of patients and relatives

Theme	Subtheme	Agree (%)		Disagree (%)		Don't know /Did not understand/ other	
		Patients (N = 8)	**Relatives (N = 10)**	**Patients (N = 8)**	**Relatives (N = 10)**	**Patients (N = 8)**	**Relatives (N =10)**
Need to test new drugs in clinical trials		8 (100)	10 (100)				
Reasons for patients to participate	Health benefits	4 (50)	3 (30)	2 (25)	5 (50)	2 (25)	2 (20)
	Monitory benefits	3 (37.5)	4 (40)	5 (62.5)	4 (40)		2 (20)
	Altruism	7 (87.5)	10 (100)			1 (12.5)	
	Trust in doctors	8 (100)	10 (100)				
	Duty to participate	7 (87.5)	10 (100)			1 (12.5)	
Doctors motives	Experimenting	6 (75)	7 (70)		1 (10)	2 (25)	2 (20)
	Career promotion	4 (50)	6 (60)	4 (50)	3 (30)		1 (10)
	Mainly to help patients	8 (100)	8(80)		1 (10)		1 (10)
Problems faced by patients	Difficult to trust doctors/ organizations	4 (50)	5 (50)	2 (25)	5 (50)	2 (25)	
	Unable to understand consent forms	4 (50)	7 (70)	3 (37.5)	3 (30)	1 (12.5)	
Problems with trials	Consume time and interfere with doctors work	4 (50)	3 (30)	3 (37.5)	5 (50)	1 (12.5)	2 (20)
	Do not address patients concerns	4 (50)	3 (30)		5 (50)	4 (50)	2 (20)
	No privacy for information	5 (63)	2 (20)	3 (37.5)	7 (70)		1 (10)
Elements of RCTs	Need for randomization	6 (75)	7 (70)	1(12.5)	2 (20)	1 (12.5)	1 (10)
	Placebos not justified	6 (75)	3 (30)	2 (25)	6 (60)		1 (10)
	Informed consent justifies RCT methods	6 (75)	3 (30)	1 (12.5)	4 (40)	1 (12.5)	4 (40)
Involving patients in designing trials not necessary		3 (37.5)	3 (30)	3 (37.5)	7 (70)	2 (25)	
Willingness to participate in placebo controlled trials		6 (75)	3 (30)	1 (12.5)	3 (30)	4 (40)	1 (12.5)
Decision to participate is a family decision		5 (62.5)	9 (90)	1(12.5)	1 (10)		

Participants also endorsed the difficulties patients faced in participation in trials with half the patients and relatives agreeing that lack of trust in the motives of the doctors and the organization doing a clinical trial would be a barrier to their participation, and three-quarters of the relatives agreeing that consent forms are difficult to understand by patients. In addition, relatives added, "…because of the audio hallucination he is not able to understand the things directly. He requires more time to understand anything and if you disagree with him on any front he gets irritated…"

"He even forgets whether he has taken the medicine or not. He cannot tell me certainly whether he has taken the medicine. This is the state of his mind, so in that case he may not be able to understand these things; that is my perception."

More patients than relatives felt that clinical trials interfere with clinical care; do not fully address patients concerns about whether the drug is effective or safe; and participation results in a lack of confidentiality (Table 2).

The methods used in trials in increase internal validity were endorsed by 75% of patients and 70% of relatives agreeing that randomisation was necessary. However, while 75% of patients agreed that using placebos in trials is not justified even if it is good way to do research, 75% agreed that if patients sign an informed consent form to participate, then randomisation, blinding and placebo comparisons are justified. The same proportions also expressed their willingness to enrol in placebo controlled trials. However, while 70% of relatives endorsed the need for randomisation, only a third agreed that placebos were not justified, or that informed consent justifies the methods used in RCTs.

Some equated randomization as luck…"We are saying that this is their luck. You have already informed that it is just like the toss. It is according to their luck."

Others were pragmatic in their approach, “Generally I think patients will not be generally willing to take part in trial medicines because what everybody wants that new medicines should come and more beneficial medicines should come, but I should not be the first to try. Let others be tried and I will take the benefit. It is the general nature of general human…Everyday, we are coming across a new antibiotic, but no person wants that I should be the first man to try with the new medicine”

“I may or may not take part that will depend upon the situation at that time… if patient is recovering well with the treatment given to him by the doctor, he may not agree for the trials, why waste time on the trials if the trials may be useful, may not be useful. Rather it may leave behind some side effects also, so why to take risk…Theoretically many things are correct, but when things come to the practical life, most of the people fly away from the scene”

“I want that only tested medicine should be used…. I do not want to take more risks..”

The majority of relatives (90%) and patients (63%) felt participation in clinical trials is a family decision. However, one mother responded:“Patient alone can take the decision. Patient’s cooperation is most important. They won’t accept when we (relatives) tell them. Even though we are accompanying them they won’t accept….”

While 75% of relatives disagreed with the notion that involving patients in designing trials was unnecessary, only a third of patients had clear opinions on this.

Comprehension of the information regarding the hypothetical RCTs

The ten questions assessing comprehension of the information provided for the hypothetical RCT were grouped as follows:

Four questions assessed the participants' comprehension on equipoise, four other questions assessed their recall and knowledge of the specifics of the design, one question each assessed their comprehension on randomization and blinding, one question assessed their appreciation of risks.**Table 2** details the proportion who provided correct responses to the questions.

Table 2: Comprehension of information regarding the hypothetical RCT

Themes	**Percentage (numbers) of patients who gave correct answers (N=7)**	**Percentage (numbers) of relatives who gave correct answers (N=10)**
Assessment of comprehension on equipoise (Questions 1, 6, 10)	43% (3)	40% (4)
	43% (3)	50%(5)
	43% (3)	50% (5)
Assessment of comprehension of randomization (Question 2)	57% (4)	30 % (3)
Assessment of comprehension on blinding (Question 4)	57% (4)	60% (6)
Assessment of appreciation of risks (Question 7)	29% (2)	30% (3)
Recall and knowledge of design (Questions 3, 5, 8, 9)	29% (2)	50% (5)
	29% (2)	60% (6)
	71% (5)	70 % (7)
	71 % (5)	40% (4)

Overall, comprehension of the essential elements of the trial was poor for all participants in general, and for patients in particular.

Comprehension of the information for the extension to the hypothetical RCT was assessed using five questions organised under three themes (Table 3).

Table 3: Comprehension of the information regarding the extension to the hypothetical RCT

Themes	Percentage (numbers) of patients with correct responses (N=7)	Percentage (numbers) of relatives with correct responses (N=8)
1.Assesment of comprehension of equipoise (Question 1)	71% (5)	38% (3)
2. Assessment of comprehension of risks. (Question 3)	71% (5)	50% (4)
3. Recall and knowledge of design. (Question 2, 4, 5)	57% (4)	75% (6)
	43% (3)	75% (6)
	29% (2)	25% (2)

Although most of the participants on enquiry, replied that they had understood the content in the information sheets, discussions revealed otherwise. The concepts of randomization, blinding and use of placebo were not understood by many in spite of the detailed descriptions given in the information sheet. Many of them preferred listening to the interviewer explaining the content of the information sheet rather than reading the sheet themselves. Fewer patients could recall the specifics of the study as compared to the relatives.

The sample size does not allow generalizing the results, but the general assessment of comprehension of patients of the concepts of equipoise, concept of randomization comprehension of risks involved was affected by their poorer ability to recall information discussed with them as compared to their relatives.

Willingness to participate in the hypothetical RCT and the extension to the hypothetical RCT

Table 4: Willingness to participate in the hypothetical RCT and its extension

	Numbers (%) of patients (N = 8)		Numbers (%) of relatives (N = 10)	
	Likely to participate	**Unlikely to participate**	**Likely to participate**	**Unlikely to participate**
Hypothetical RCT	3 (37%)	5 (63%)	5 (50%)	5(50%)
Extension RCT	4(57%)	3 (43%)	4(44%)	5(56%)

Overall about fifty percent of the participants were willing to participate in either of the trials.More patients were willing to participate in the second RCT which required the continuation of usual drugs along with the trial medication without a wash-out period without medicines.

The qualitative data for the discussions held towards exploring the reasons for participation were grouped under the following themes:

Reasons for not participating

Cognitive deficits were quoted as the reason by one patient, “Because I am forgetting everything… what I am reading… how can I remember the name of the drug or the chemical…I will not be able to write and give the side effects…”

Side effects: “I do not feel like going into any new medicine trial. The medicines, which are already proved right and is generalized that had so much adverse effect on me that I dare not to go on any medicine that is not yet proved.”

“I am already known of the fact that my body is so much sensitive to the psychotic medicine, how can I go with the trial? It makes sense? how can I go with the trial?”

“One thing is sure any psychotic medicine does not have good side effect. It is bound to trouble the patient and during my experience in this field in the last two years with my son, I have come to learn this that no psychotic medicine has good side effect”.

“When I do not have any option, we have to treat the patient to get him cured. Along with the recovery, he also happens to get some (side) effect. Then somewhere we have to make the compromise and let this compromise be made with the known medicines…known and tested,… that is my personal opinion.”

“(relatives) would fear that her other problems might increase or maybe that medicine may not go hand in hand with whatever medicines she is taking…Or maybe (she may have) some type of side effects”

Lengthening of the hospital stay:

“Once my patient takes part in this study, the usual medicines with be withdrawn temporarily and he will be put on new medicines. This is likely to lengthen the treatment period here. That I cannot afford. This is the first reason to refuse the participation”

“even for the four weeks suppose if they have got an option that just for the trial we have to stay for four weeks then maybe most of the people will say no unless they live nearby.. Who will spare one month just for your trial?”

The drug tested being inappropriate for the primary disease:

"he is already suffering from schizophrenia of perhaps the high degree and this medicine is not meant for schizophrenic symptoms. This is only meant for stress, so this medicine may not be useful for his original disease."

"if we consider the present condition of (the patient) and then judge this medicine then maybe it does not suite her requirement"

Stopping of usual medication:

"What has made me to make the decision that at this stage(he) will not be going for any clinical trial simply because it will remove all the medications that are being given to him. This will bound to create problems…Stopping altogether the current medicine and putting the patient on the new medicine. That would have jeopardized the whole current treatment process.…"

"…to do this trial, the other medicine maybe whatever she is taking, would be reduced. Neither doctors maybe agree and maybe we will also not agree".

"Doctors have told us to continue medication. Now you are saying medication will be stopped… now I am scared that the similar illness will come back…"

"if my usual medicines is not given my problem may not reduce."

If the current medication is stopped I am scared about what will happen…"

"He cannot miss this medicine..which is brain medicine for a single time… it must be regular wherever you go… my confusion is.. if that is stopped, will problem arise…"

Treating doctors would not recommend stopping medication

"What is the purpose of the trial, whether to make her better or to make this trial a successful one? Because seeing her condition I don't think the doctor will say yes (to stopping medication)…"

"I know such a situation will not arise because what is technically possible that only will be advised by the doctor."

"Patient is eating the medication her doctor has given…in between if we go and join this trial… how will we answer them….?"

Severity of the current illness

"Because my patient at this stage is in a critical condition, I already lost about two years in treatment and now I do not want anymore experiment regarding the medicines. What I want only tested medicines should be used in this case.."

"I myself am in such a worsened condition… suppose it gets even worse after I take the ordinary tablets…"

"Maybe (if) her condition was not so severe, and if the doctor would have recommended, we may have gone for that (the trial).."

Other treatment options being available

"I could have agreed to this trial test had there been no other options left for me, but as on date I think they are certainly other options available, so at this juncture I am not prepared to let my boy participate in the trial."

"At present if we are trying clozapine on her. Like, suppose after one year, we find that is also not working… Then, we will say yes because we don't have any other

options.(but)now when she is already being tried on clozapine and if you say okay for our research purpose let us try this medicine, I will say sorry.."

"Even if the doctor recommends I won't take part..now I am better .. now why should I try other medicines?"

Blood tests:

"Ddifferent types of tests are to be carried out during entire procedure. That is certain to put extra burden on the patient Psychological load on him …."

"Sschizophrenia is such a disease that I cannot predict whether if he agrees today, he may not agree tomorrow. Once he sees that EEGs and ECGs are being conducted on him, he may think that trial itself is false and actually being treated differently for earlier disease. These things may come in his mind"

However, some opined that blood tests were not a problem: "I have given blood earlier and I know that that is not a big issue, so it does not matter."

"Not much concern..because even for the normal treatment blood tests are done."

" blood tests are very simple… no problem to health…these are the usual tests done .. so no problem…"

"I am afraid of needles… even if I had malaria and was sick I would not give blood tests… but I will agree to it for her(patient) because I want her to be well…"

Family disagreeing

"My wife is not going to agree. Mothers are more possessive of their children..more concerned. I think in general. Father may take some risks, but mothers will not. It may or may not have a detrimental effect, but she will never agree. She may not think

in broader terms that I do have the courage at times to think over… I think this scenario exits in every Indian family".

"But as I am under the parents, I will listen to what they say. I don't think they are interested…"

" (if)you have signed the consent slip maybe even with their(family members') consent, but afterwards the family members say I was telling not to go for that. Who will answer them if something goes wrong? Then, how you will be able to face them? They will accuse you. Nobody would like to get accused…"

"I can say only after I ask my husband…."

"Once we join the trial you want us to come back… but will her husband allow her to be brought… I don't know I can decide only after asking her husband.. I cannot do anything without asking him…"

"If I take a decision alone and something happens then my husband will ask me why I did not enquire of him.."

Inconveniences

"I am from a faraway place… there are children at home… we cannot come for these trials…"

"I cannot take part in this research. Because I am having children, if I participate nobody is there to stay with me. I have to stay alone. My health condition is not good. Nobody is there. Today my brother is here. He cannot stay because he has to go for work.."

"We cannot stay here for four weeks… even getting meals here is expensive… my husband staying at home also is eating from a hotel…"

Personal 'weakness'

"Situation is very paradoxical actually. Only trial that is carried out on animals, mouse, cats, is not enough for the medicine to be tried upon the human.Still everybody does not have that much courage to participate. Maybe, I am weak there…You will find many more persons like me. You may find many brave persons who would like to encourage in the tests, but the number is perhaps less in India and perhaps this is the reason the Indian scientists have not been able to bring forth new medicines at the rate expected of him"

Lack of education

"Because knowledge is less; there are less educated people. There are more illiterate people. 'why should we come forward first?' that sort of attitude' also spreads to educated people…"

"the education level and era comes in. The people of this era..who have some scientific background or who know that some researches are necessary may say yes, but it could be very difficult to convince the fathers and grandparents and all that"

"because people who know that these are the research, this is the science and all that will not be afraid… so the education plays a lot of role…"

Randomization

" i can only take the medication I choose…"

Some thought of it as 'luck' and 'athishti', "if you don't know and I don't know (what medicine will be given)… then it is our luck…I don't have a problem with that…"

"I wont know what medicine I will be taking… that will be difficult for my health…"

"my doctor knows my condition, so if my doctor does no thave a choice in (what medicine I will get) my health will become worse"

"If doctors are not sure of what medication will be given them I am scared"

Reasons for participating

Altruism:

One patient opined, "It is for a good cause that's it. I am in a situation to be participating in this to get a good solution to a problem, but whereas other people may not begin, but they might be requiring it, so in that case I can help them out..helping people that's the sole motive for me, at least for me …."

"Participating will provide a new medicine for other people. This can help other people"

"I am interested that's why I have (consented)… if some part of the distress (for a psychiatric patient) is abolished then what s the harm in that..he will be relieved…"

"It is my nature… I like new things to come… if it is successful it will give a new turn to the lives of the patients…"

Personal benefits

"Personally do, yeah because if I get to suffer that sort of a disease in future, maybe I might be getting those medicines too to sort out this problem. Who knows?"

"Food also needs to be given… you are providing for conveyance, lodging… food also has to be provided"

"Some monetary compensation must be there from the research side..he is volunteering to give so many tests…he must get a medal at least…"

Trust in doctors

"Doctors won't stop(medication) for nothing. There will be a reason behind it and that would not let me down that much. That belief in doctors helped me arrived at the conclusion. I firmly believe that doctors will help me to come out of a problem if it arrives... "

"Everything can be done on the patient if the doctors suggest it is good to go for it.."

"I may not have a problem. I see earlier the research and all are very authentic and if the doctor recommends"

" I am not worried (about dummy medicine)…. You (doctor) know about it…the side effects of the dummy tablet, or the side effects of GVV tablet is known by the doctor… I don't know. And doctor (should) what should be taken."

"Doctor's choice is perfect…"

" I will ask you to do whatever you wish…we don't know what medication should be given to whom… but you (doctors) do, and you are taking care of crores of people…"

" if anything to be scared of was happening in this hospital would so many people be coming here?…."

"Anyway doctors will take care… whatever you give is like God has given…."

"If anything happens after giving the dummy medicines , the doctors only will take care.. so I am not scared… you (doctors) can do everything.. we can do nothing…"

" because you are asking I will agree… I feel that you will not ask me to do something that will harm my daughter. So with that trust I am agreeing to participate. I believe you will want to do only what is best for me."

"Whatever you do you are doing as doctors.. so if it is good or bad we will accept it…whatever the doctor gives it will be for the patients good and so we will accept it…"

Recommendation of the treating doctor

"If the treating doctor recommends we will participate madam… nothing else needs to be asked..we will join…"

Monetary benefits

A patient opined:"You said "your stay will be free of cost for the four weeks you stay here" that helped me to arrival of this decision because we are not that well off to pay for stay for a long period of time. It was a good incentive that helped me to arrival of this decision…"

"I am probably likely to participate in this trial provided I am not disturbed monetarily…"

Choice between the first and second study

Many of the patients favoured the second study because the usual medication would be continued:"Because required medicine will go on regularly and the new medicine also be tested, but in the former one the medicine will be completely stopped and the level of the medicine in the brain will get down, so all the hard work from two to three months will go in vain".

"surely (the trial)in which the usual drugs are continued. It would be always liked if the usual drugs are continued.."

Opinions on patients participating in designing trial

"These studies are done on patients… so they have to help design trials…".

"One or two people..who you think are credible.. maybe 30 percent of the people participating.. they may give economical, theoretical points or research related points …"

Other factors influencing the choice:

The fact that the medication came from outside India, "the persons willing to go in trial I think will be 1/10 persons...Because it is risky. So many side effects can occur. We do not know anything. This is coming from outside India. Why they are experimenting in our country? Why are they not experimenting in their own country? You test on your own people and then it will be okay, then send to my country".

"Medicines are being supplied from Switzerland…. Suppose due to some reason, the supply of medication gets stopped. Then what would happen to the patient?"

Another relative felt it was good if the drug was imported, “it doesn't matter, the medicine from Switzerland is good. Indians would like imported, so if it is from Switzerland, it is good”

Other issues

Some patients had difficulty expressing the reason for a choice:“..no reason.. I cannot express…”

Some had never heard of research, “ I have never even gone to a hospital before.. I have delivered five children but still have never been to a hospital… I have not heard of such things as research and testing medication…”

“I have not heard of such things as research and trials…”

“I don’t know…I won’t join.. I don’t know why.. I am scared if some problems will arise…I don’t know how to say…”

“I cannot understand why you are asking questions like this….”

“It is difficult for me to answer these questions you are asking…”

One relative mentioned, “I don’t mind participating In a real trial..but I must get a confident reply on an authenticated document undertaking that the trial is conducted and we will give you the patient the same.. back.. “

Opinions regarding dummy medicine

“What dummy medicine?... “dummy”.. that is not medicine… that is called poison… it gives harm to the patient.. you have written “dummy”.. the word gives me more pain…”

“Madam whatever medicine you give her she must become normal. if she goes back to her previous state it is scary isn’t it …its three months since we came here and now she is better.. if you now give her dummy medicine and then something happens.. Then?”

“I have no concerns about he dummy tablets. It is not in anybody’s hands..”

“All these tablets are related to the brain..if something.. even a small chemical reaction happens in the brain…I am scared of what will happen…”

“Do not give dummy medicine. What is in use of giving the dummy medicine? It won’t work in the patient’s body. There is no chance of curing. Then what is the use? …” .

Observations noted during the conduct of the interviews.

Field noted were maintained as a part of recording the context and other non-verbal behaviour which was noted during the process of the interviews. In one instance, the patient who was during the informal rapport building session judged to be competent, became disturbed and started behaving inappropriately during the interview. This happened after administering the attitude questionnaire and due to this the interview had to be discontinued.

In another instance, after one session of the interview, the patient was unable to judge the study as an imaginary study and expressed a strong desire to the relatives that he wanted to join the trial. The relatives were upset due to the change in behaviour of the patient following the discussions and requested that the discussions be stopped.

Objective assessment of competence: the MacCAT-CR interview results

We completed in total 5 MacCAT-CR interviews; twowere with patients and relatives for the first as well as the extension to the hypothetical trial. One of the relatives did not take part in the interview for the extension RCT because of impending discharge from the ward. The other relative of the patient did not give consent to interview the patient as he felt the patient was not competent to undergo such "complex" interview process. This patient was clinically also found to be incompetent later during the process. The 3rd patient could not undergo the MacCAT-CR interview as the patient became physically ill and had to be shifted to the medical ward at the time of the scheduled interview, but the relative could participate.

Table 5: Results of the MaCAT-CR evaluations

RCT	Serial No	Understanding; Relative N (%)	Understanding: Patient N (%)	Appreciation: Relative N (%)	Appreciation: Patient N (%)	Reasoning Relative N (%)	Reasoning: Patient N (%)	Choice: Relative N (%)	Choice: Patient (N%)
Hypothetical RCT with the placebo arm.	1	17(65%)	4(15%)	4(66%)	0 (0%)	4(50%)	2(25%)	2(100%)	2(100%)
	3	24(92%)	21(80%)	6(100%)	5(83%)	7(87%)	3(37.5%)	2(100%)	2(100%)
	6	5(19%)	25(96%)	2(33%)	5(83%)	2(25%)	2(25%)	2(100%)	2(100%)
	8	23(88%)	-	6(100%)	-	6(75%)	-	2(100%)	-
	13	20(77%)	-	3(50%)	-	2(25%)	-	2(100%)	-
Hypothetical RCT (extended part)	1	15(57%)	1(4%)	2(33%)	0(0%)	4(50%)	0(0%)	2(100%)	2(100%)
	3	26(100%)	20(77%)	6(100%)	5(83%)	6(75%)	3(37.5%)	2(100%)	2(100%)
	6	-	20(77%)	-	5(83%)	-	2(25%)	-	2(100%)
	8	24(92%)	-	6(100%)	-	4(50%)	-	2(100%)	-
	13	8(30%)	-	3(50%)	-	1(12.5 %)	-	1(50%)	-

(%) reflect the percentage of the total score obtained for the domain

Since the cut-off scores have not been validated in the Indian population, the scores were evaluated in four ways:

1. The proportion scoring 50% or more on the four domains of understanding, appreciation, reasoning and expressed choice to be subsequently judged as competent:

   The basic expression of choice is unequivocal and clear in both patients and their relatives; whatever be their choice.Understanding and appreciation of the concepts of the randomized controlled trial of both the placebo and extended arm was found to be overall adequate.The reasoning domains especially with patients were found to be much below the level of acceptable 50%. Both consequential and comparative reasoning was found to be inadequate.
2. The performance of participants' competence was evaluated using stringent standards (adequate on all domains): Two relatives (nos 3, 8) was competent using this standard for both trial scenarios, while another relative (no 1) was less competent to consent for the extension RCT than the first RCT. None of the patients met this standard.
3. Using intermediate standards (adequate on three domains: Understanding information, appreciation of the significance of the information, reasoning with the information) No patient was judged competent with this intermediate standard.
4. Using the least stringent criteria (Understanding information). One patient (No 1) and one relative (no 6) were found not competent even using this least stringent criterion.

   Clinical assessment of competence had found all these participants to have adequate capacity to consent.

Discussion

Summary of the results

Attitudes towards randomized controlled trials:

The general attitude towards trials was positive in the patients and their relatives and all the participants acknowledged that it is necessary to test new medication before they are made available for general use.

Trust in doctors was a very notable recurring theme in all discussions. All of them agreed that trust in doctors and the organisations where research is done was very important for participation in trials.

Willingness to participate in a hypothetical randomized double blinded placebo controlled trial

Overall the results showed that only about 50% of the participants were willing to participate in the hypothetical trial. This shows a similar trend as compared to the rates discussed in literature including a study conducted in a tertiary care setting in India [72].Possibility of side effects, both known and unknown, and the possibility of worsening of the disease on stopping regular medications are important issues that play a role in the acceptability of trials especially in the psychiatric population. Placebo controlled trials which require a drug washout period are hence perceived as a hazard by many participants. During the regular inpatient treatment in hospital much importance is given to ensuring compliance in people with psychiatric illness. Researchers approaching patients for trials which recommend a washout period may be perceived as going against the principles of beneficence upheld by the treating team. This could create confusion in the minds of people with regard to the motives of the research. Hence much care and thought has to be given with regard to discerning

between psychiatric conditions in which placebo controlled trials would be not just ethical but also acceptable to the participants in terms of safety and risks, and those conditions in which risks expected are unacceptable. This also highlights the importance of ethical issues in clinical care being not considered separate from those in research and highlights the role of "therapeutic misconception" influencing patient perceptions of interventions offered in clinical trials [41, 50].

Perceived barriers and facilitators affecting participation in randomized controlled trials

The meta-analysis by Shah and colleagues [69] includes expectation of benefits related to health, altruism, faith in doctors, expectation of additional income, thorough information about trials and methods for inspiring participants as factors favouring participation in trials. Distrust in organizations conducting trials, concerns about usefulness and risks of trials, psychological issues, trial burden, loss of confidentiality, dependency related factors, and problems related to the language of communication were quoted as the barriers to participating in trials.

Similar results were shown in our study with regard to trust in the doctor and altruism as factors improving participation. Other recurrent themes discussed as reasons for not participating in the hypothetical RCT were the severity of the illness, the fact that other already proven options were available, and that the decision required consultation with other members of the family.

Issues related to informed consent in patients suffering from psychiatric illness

Comprehension of the participants

Acceptability of trials could be improved if informed consent is considered as a process rather than an event marked by the signing of a form. Including verbal interactive discussions as an adjuvant to written information would aid in encouraging

clarification of doubts, dispelling unfounded fears and improving participation.Problems related to recall of specifics regarding the study were found to be more among the patients as compared to relatives. This may be due to the residual deficits associated with the disease but further research is required to explore the presence of other factors contributing to the same.

Even among relatives about half the participants were unable to understand the concepts involving randomization, equipoise and blinding.

Among patients, the understanding of equipoise was better following the discussion in the extension RCT as evident by the increased percentage of patients who answered correctly. This could point to the advantage of repeated explanations.Assessment of the comprehension of risks also showed better scores in the extension RCT as compared to the first hypothetical RCT.

Assessment of Competence of participants

In this study, the clinical assessment of competence of the participants was done first during the rapport building time prior to the interviews. Patients who were initially assessed to be competent by this method were later on found to be not competent during the discussions necessitating a discontinuation of the interview. Competence is a complex construct which encompasses multiple dimensions requiring formal assessment. Formal assessment of competence should be an adjuvant to the mental status examination in declaring a patient to be competent or non-competent. Issues regarding whether the process of discussion regarding the trial are anxiety provoking and stressful need to be further explored since competence is assessed in the context of the decision-making process.

The assessment of competence in this study was done clinically on the basis of the degree of comprehension of the patients and their relatives of complex constructs of

research which they had never heard of before in a tertiary care setting wherein they had come to seek treatment. Whether this was an important factor because of which many patients and relatives were judged incompetent needs to be seen in a larger representative sample. More so because the objective assessment of competence using the MacCAT-CR in a subset found most to bedeficient in consequential and comparative reasoning processes. The fact that almost all could express their choice in-spite of this deficit might point towards the fact that a lot of people including patients and relatives take decisions based on trust rather than logical reasoning process.

The findings from this study point to the need for a more comprehensive method of assessing competence which would add on to the mental status examination in declaring a participant as competent or not. Assessment of the relatives for competence in understanding the issues involved in RCTs may also be required in view of the fact that in this study many of the relatives also were found to be not competent at the end of the discussions.

The justification of the methods used for the study.

There is a need for more information on the subjective perceptions and opinions of people with psychiatric illness about randomized controlled trials. The attitudes of the patients and relatives towards these trials need to be explored to identify common issues which can be addressed to improve participation in future. Cultural differences in attitudes are also important.

Qualitative research methods are known to enable a rich descriptive understanding into the complex aspects of subjective experiences. The “Prospective preference assessment” method provided a framework within which the willingness to participate in trials could be assessed and qualitative methods of face to face interviews enabled

exploration into the reasons regarding the choice to participate or decline. These were combined with quantitative assessments of the willingness to participate and the competence of participants to further address issues related to informed consent and assessment of competence.

The transferability of the results

Patients were recruited from a tertiary care inpatient facility. Since such patients are likely to be the ones approached to participate in research and since they are also more likely to have impaired decisional ability than outpatients, the result of this study would have value in applicability to other similar settings in India. The opinions of their relatives are also likely to reflect those of relatives in other settings. The concerns regarding people with psychiatric illness are very different from those of patients with other physical illness and the study has attempted to identify these issues. The perspectives and opinions of relatives of patients with psychiatric illness are also different from the general population and this study tries to highlight the complex nature of the issues faced by them in consenting to allow their relatives to participate in randomized controlled trials.

Limitations of the study

The lower than expected recruitment into the study resulted in suboptimal numbers of participants providing data from this study to adequately inform attempts to improve the understanding of factors important to patients and relatives regarding trial participation. Rapport was a very important factor deciding the quality of the data. In cases where rapport was difficult to establish with the participants the quality of the interview was compromised.

A hypothetical RCT was used to find out the attitudes and willingness to participate and this may not exactly reflect the opinions of those who are actually called for real

trials. However, the responses of participants are indicative of a cross-section of opinion of potential trial participants.

Due to time constraints the translations of the Tamil version of the questionnaires and interview guides could not be back translated into English. However in most cases when Tamil was the medium of communication, the participants requested the investigator to explain to them the content in the questionnaire and consent forms and did not prefer to read it on their own.

The attitude questionnaire was not a validated tool, but since it was not designed to give a score, rather was used as an aid in guiding discussions on required topics.

The voice recordings for one participant (serial no.18) were of poor quality and hence could not be transcribed.

Data from a few Tamil and English files could not be transcribed completely in time and hence only relevant parts were transcribed into English.

This study did not aim to make formal correlations between psychiatric symptoms, cognitive impairment, and competence to provide consent. Hence more appropriate tools for formal assessments of psychiatric symptoms, and cognitive deficits were not used to make such evaluations.

Strengths of the study

This study was designed according to the COREQ standards for qualitative studies and also provided quantitative data and included detailed transcripts of audio-recorded interviews.

A number of steps were taken to minimise biases. Selection bias wasaddressed by consecutively assessing all admitted patients into the study who fulfil the eligibility criteria and consented. Representativeness was addressed by ensuring that at least half the patients have a psychotic condition and the remainder will comprise non-

psychotic conditions; all participants will have a CGI score of at least moderately ill. Bias due to the nature of the acute illness reflecting in lack of capacity to consent was dealt with by repeating the consent assessment after an additional week in those felt on clinical assessment to lack the capacity to consent.

The structured MacCAT-CR manual and scoring were kept away from the primary investigator, who assessed competence using clinical assessment that is used routinely in clinical care. While, the domains of the MacCAT-CR are known to to the investigator, the relative importance given to each domain while scoring, and the structured manner in which the MacCAT-CR is used differed from a clinical assessment of competence.

All the instruments used for this study were assessed for cultural and linguistic appropriateness and pilot tested with records made of any alterations.

Field notes were kept during interviews to record contextual data.

Recording the interviews and evaluation by an independent professional helped minimize ascertainment bias and bias due to erroneous interpretation and recall, and also served as a quality assurance measure.

Conclusions

This cross-sectional study using quantitative and qualitative methods and using the Prospective Preference method to ascertain the views of psychiatric patients and their relatives towards participation in clinical trials revealed that while patients and participants consider it necessary to conduct RCTs for scientific purposes and consider participation in these trials as an altruistic imperative, and the methods of RCTs that increase internal validity appropriate; their willingness to participate in such trials are likely to be increased by trust in their doctors and the organisations they represent, as well as by personal health and financial benefits, and the opinions of family members; and reduced by a variety of factors that include potential risks and burdens associated with trial participation. Comprehension of information required to provide valid consent is likely to be sub-optimal, but could be enhanced by conversation and repeated explanations, supplementing written information. Even then, roughly 50% approached to participate in such trials are likely to refuse participation. The prospective preference method has value in informing the design of future trials. Finally, formal assessments of the capacity to consent is routinely recommended in trials involving psychiatric patients, even if clinical assessments indicate that eligible participants have the capacity to consent to participate in clinical trials.

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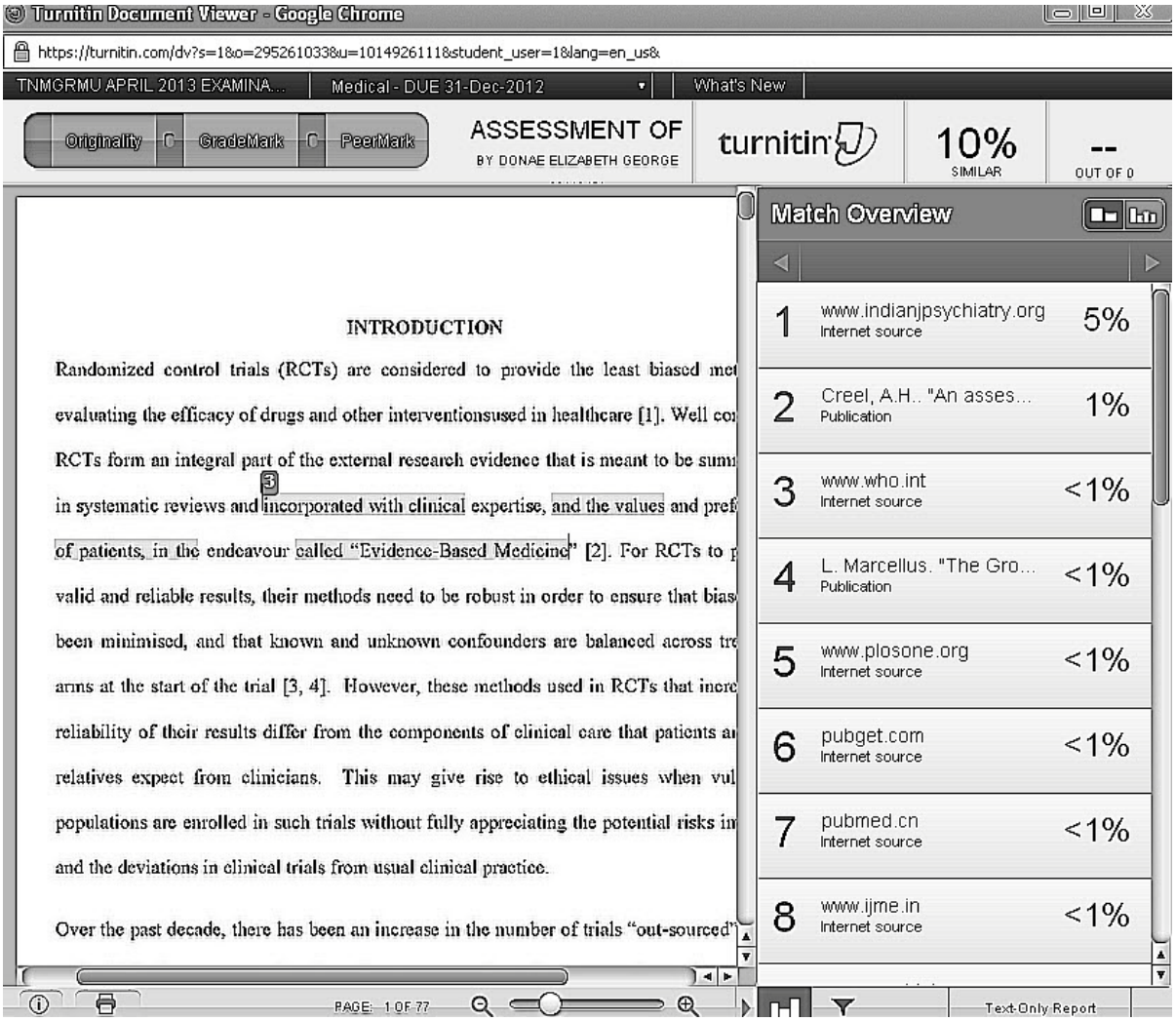
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INTRODUCTION
Randomized control trials (RCTs) are considered to provide the least biased met
evaluating the efficacy of drugs and other interventionsused in healthcare [1]. Well co
RCTs form an integral part of the external research evidence that is meant to be sum
in systematic reviews and incorporated with clinical expertise, and the values and pref
of patients, in the endeavour called "Evidence-Based Medicine" [2]. For RCTs to p
valid and reliable results, their methods need to be robust in order to ensure that bias
been minimised, and that known and unknown confounders are balanced across tre
arms at the start of the trial [3, 4]. However, these methods used in RCTs that incre
reliability of their results differ from the components of clinical care that patients a
relatives expect from clinicians. This may give rise to ethical issues when vul
populations are enrolled in such trials without fully appreciating the potential risks in
and the deviations in clinical trials from usual clinical practice.
Over the past decade, there has been an increase in the number of trials "out-sourced"
PAGE: 1 OF 77
Match Overview
1 www.indianjpsychiatry.org Internet source 5%
2 Creel, A.H.. "An asses... Publication 1%
3 www.who.int Internet source <1%
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Text-Only Report

INSTITUTIONAL REVIEW BOARD (IRB)
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Editor, Indian Journal of Psychological Counseling
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Chairperson, Research Committee &
Principal

Dr. Nihal Thomas
MD, MNAMS, DNB(Endo), FRACP(Endo), FRCP(Edin)
Secretary, Ethics Committee, IRB
Additional Vice Principal (Research)

July 3, 2012

Dr. Donae Elizabeth George
PG Registrar
Department of Psychiatry
Christian Medical College
Vellore 632 002

Sub: **FLUID Research grant project NEW PROPOSAL:**
Assessment of attitudes towards participation, willingness to participate, and competence to participate in Randomized Controlled Trials: a cross-sectional qualitative and quantitative survey of psychiatric patients and key family members using the "Prospective Preference Assessment" method and the MacArthur Competence Assessment Tool for Clinical Research (MaCAT-CR). Dr. Donae Elizabeth George, PG Registrar, Psychiatry, Dr. Prathap Tharyan, Dr. Saumil Dholakia, Psychiatry.

Ref: IRB Min. No. 7825 dated 18.04.2012

Dear Dr. George,

The Institutional Review Board (Blue, Research and Ethics Committee) of the Christian Medical College, Vellore, reviewed and discussed your project entitled "Assessment of attitudes towards participation, willingness to participate, and competence to participate in Randomized Controlled Trials: a cross-sectional qualitative and quantitative survey of psychiatric patients and key family members using the "Prospective Preference Assessment" method and the MacArthur Competence Assessment Tool for Clinical Research (MaCAT-CR)." on April 18, 2012.

The Committees reviewed the following documents:

1. Format for application to IRB submission
2. Cvs of Drs. Donae Elizabeth George, Prathap Tharyam, Saumil Dholakia.
3. A CD containing documents 1 - 2

TEL : 0416 - 2284294, 2284202 FAX : 0416 - 2262788, 2284481 E-mail : research@cmcvellore.ac.in

INSTITUTIONAL REVIEW BOARD (IRB)
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MD, MNAMS, DNB(Endo), FRACP(Endo), FRCP(Edin)
Secretary, Ethics Committee, IRB
Additional Vice Principal (Research)

The following Institutional Review Board (Ethics Committee) members were present at the meeting held on April 18, 2012 in the CREST/SACN Conference Room, Christian Medical College, Bagayam, Vellore- 632002.

Name	Qualification	Designation	Other Affiliations
Dr. B. J. Prashantham	MA (Counseling), MA (Theology), Dr Min(Clinical)	Chairperson(IRB)& Director, Christian Counselling Centre	External
Mrs. S. Pattabiraman	BSc, DSSA	Social Worker, Vellore	External
Mrs. Ebenezer Ellen Benjamin	MSc. (Nursing)	Maternity Nursing CMC.	
Dr. Vathsala Sadan	MSc, Ph.D	Community Health Nursing CMC.	
Mr. Samuel Abraham	MA, PGDBA, PGDPM, M.Phil, BL.	Legal Advisor, CMC.	
Mr. Joseph Devaraj	BSc, BD	Chaplain, CMC	
Dr. Nihal Thomas	MD MNAMS DNB(Endo) FRACP(Endo) FRCP(Edin)	Secretary IRB (EC)& Dy. Chairperson (IRB), Professor of Endocrinology & Addl. Vice Principal (Research), CMC.	

We approve the project to be conducted as presented.

The Institutional Ethics Committee expects to be informed about the progress of the project, any serious adverse events occurring in the course of the project, any changes in the protocol and the patient information/informed consent and requires a copy of the final report.

Yours sincerely,

Dr. Nihal Thomas
Secretary (Ethics Committee)
Institutional Review Board

Secretary
Institutional Review Board
(Ethics C ittee)
Christian M al College
Vellore - 632 [illegible] Tamil Nadu, India

TEL : 0416 - 2284294, 2284202 FAX : 0416 - 2262788, 2284481 E-mail : research@cmcvellore.ac.in

Appendix 1a

INFORMATION SHEET

Title of the study :

Assessment of attitudes towards participation, willingness to participate, and competence to participate in Randomized Controlled Trials

Name of the investigators and institution:

Dr. Donae George; Dr. Saumil Dholakia; and Dr. Prathap Tharyan; Christian Medical College, Vellore.

Invitation to take part in a research study

My name is Donae George and I am a doctor working in this hospital. I am approaching you to help me with my research study that I am doing as part of the training for my MD degree in Psychiatry. I am inviting you to participate in this research study and wish to provide you with information about this study. I hope that you will give me your permission to participate in this study after you have understood what this study is about and what you will be expected of you, if you decide to take part in this study.

This information sheet provides details of the proposed study and I request you to go through this information and allow me to answer any questions you may have about this study, before you make your decision. Your decision on whether you will or will not participate is entirely up to you. Taking part in this study does not form any part of the treatment being provided at this hospital. Whether you decide to take part or not take part in this study will not affect the treatment you will receive at this hospital.

The doctors who are treating you are aware of the details of this study and have permitted me to invite you to consider taking part in this study. This study has been approved by the Christian Medical College and Hospital. Dr. Saumil Dholakia, one of the consultants working at this hospital, is helping me with this study and Dr. Prathap Tharyan, a Professor of Psychiatry at this hospital is supervising my work.

What is the purpose of this study?

In this study we aim to interview 30 people with psychiatric problems admitted to this hospital and one relative of each of these patients. The purpose of this study is to understand the opinions of people with psychiatric problems and their families about taking part in research involving new medicines used to treat psychiatric conditions.

What kind of research is used to study new medicines?

Any new medicine that is being considered to be approved by the government to treat people with any medical or psychiatric problem needs to be first tested in research studies on people with that condition. This research first involves studying the effects of this medicine in the laboratory and later on a few people to find out what the dose to be used is, and whether it is safe to take this new medicine. Once this is done, the new medicine is then again tested in many more people by comparing the effects of this medicine in people with the medical or psychiatric problem who take them and in people with the same problem who are not given this medicine. This is the only way that we can be sure that whatever any improvement or problems reported by people on the new medicine is actually caused by the medicine and did not happen by accident, or by chance; or due to any other reason.

One of the other reasons why the new medicine may appear to be better or not as good is because the doctor selected the people into the study in a particular way; those selected people who got the new medicine were either more or less sick than people who did not get the medicine at the start of the study. It is important to make sure that the effects of the medicine are clearly due to medicine itself. The method used to do this is to choose each person by a coded system similar to a lottery, or like tossing a coin. This method will help to make sure that everybody in the research study has an equal chance of getting the new medicine or not getting the new medicine. The doctor does not directly decide what treatment the patient gets and the patient cannot chose whether he or she gets the new medicine or does not get the new medicine.

However, the doctors and people who do not get the new medicine might come to know as these people would see other people who got the new medicine either feel better or develop side effects To prevent this from happening, those who are not selected to get the new medicine will get an identical looking medicine that does not contain the new medicine, but contains a powder that has no bad or good effects (a placebo or a dummy medicine). Because it looks and tastes identical to the new medicine, the patients and the doctors treating them will not know who is taking the real medicine and who is taking the dummy medicine. If we do not use these methods in research studies before we prescribe them in larger numbers, we cannot be sure that new medicines really work. Most of the medicines all of us take to treat different problems have been tested in similar research studies where other people have agreed to take part even though they did not know exactly what medicine would be given to them. All of us who have taken treatments with medicines have benefitted from the actions of those people who took part in such research studies.

Because these research studies (called Randomized Controlled Trials or RCTs) are different from what happens when people normally go to doctors for treatment, it is important that people understand the differences. It is also important that they give their permission to take part in such research studies voluntarily and after knowing the details of the study. The difficulty is that since people are so different, not everyone

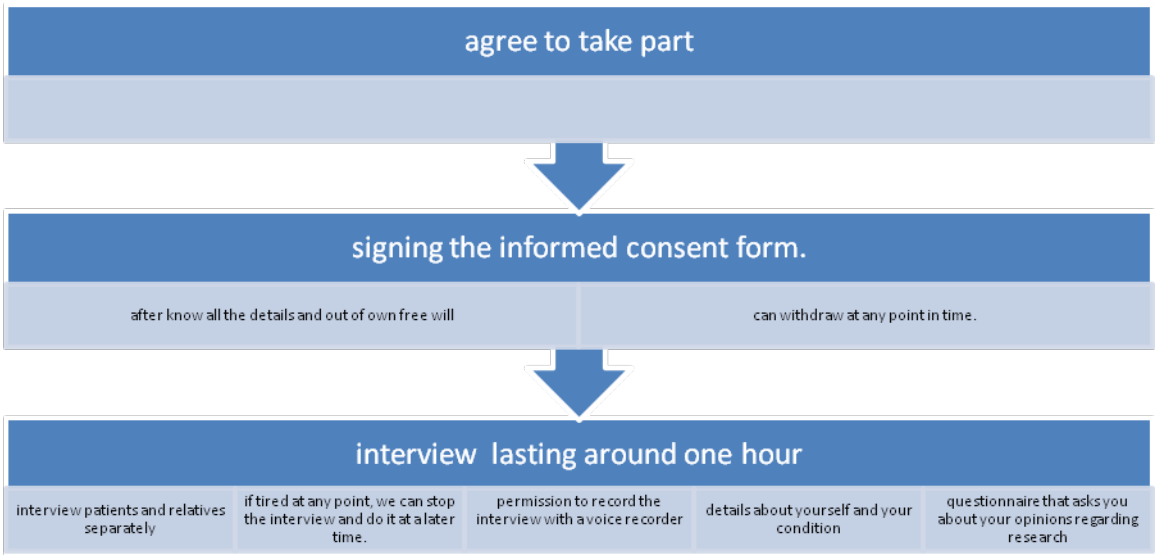
may want to take part in these studies and not everyone may be able to understand the details of such studies. Some people may also be more willing to take part in such studies if the details were explained to them to their satisfaction and if the researchers understood the difficulties and concerns of patients who participate in research, and if the RCTs were designed in ways that helped patients who take part.

The research study that I am doing does not involve actually giving you any medicines. In my research, I wish to find out your opinions about such research studies so that this information will help us understand how to do them better in the future.

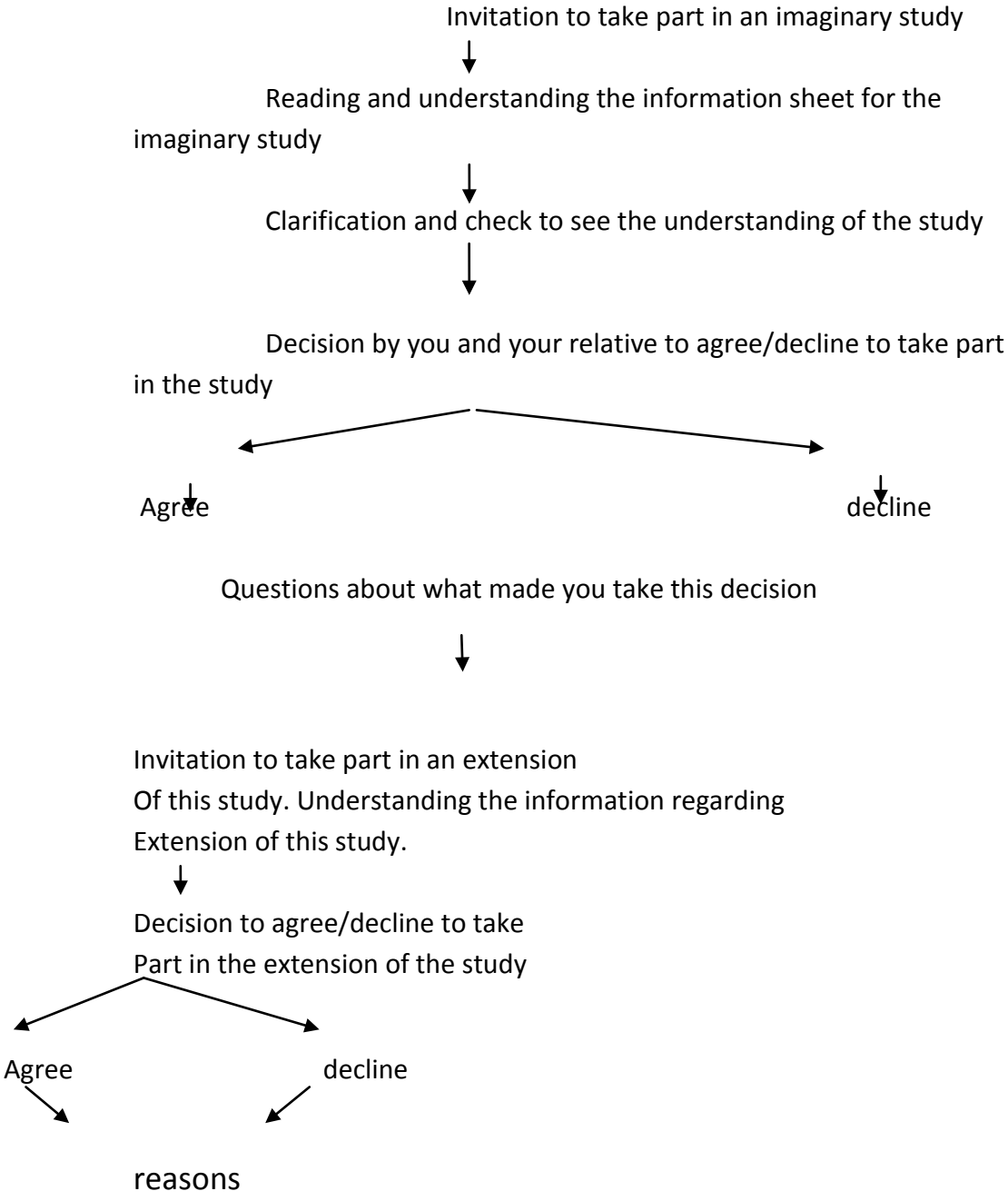
What will you have to do if you agree to participate?

There are three parts of the study. The first and second part will be conducted by me and the third part by my colleague Dr. Saumil dholakia.

Part 1: flow chart.



Part 2



If you agree to take part in this study, I will first request you to sign a form that states that you agreed to take part in this study out of your own will after understanding all the details of this study, and were not forced to take part. This does not mean that you cannot withdraw your permission at any time after signing the form as it is only meant to make sure that doctors do not do research on people without their permission.

I will then interview you in a private place and this interview may last for roughly one hour, though it may take less time or more time, depending on how easy or difficult it is for you to understand the questions you are asked. If you feel tired at any point, I will stop the interview and we can do the remaining part of the interview at a later time. I will interview patients and relatives separately unless you specifically wish for your relative to be present with you.

In order to make sure that I do not forget what you said during the interview or that I do not make mistakes about what you said during the interview, I request that you permit me to record the interview using a voice recorder. This will permit Dr Prathap Tharyan, my supervisor, to listen to the interview and check any mistakes in my impressions about the interview. By listening to the recordings of the interviews of all the people who take part in the study, we will be able to compare opinions, and identify common concerns or view-points. This will help us improve our understanding and will help us make better conclusions about this research. You will not be personally identified in this recording and I will give you a code number so that nobody actually knows whose voice was recorded apart from me.

I will ask you (if you are a patient admitted to this hospital) details about yourself and your psychiatric condition and treatment. If you are the relative of a patient, I will also ask you details about yourself and your relationship to the patient. I will write down this information.

I will then give you to read, and also read out, a questionnaire that asks you about your opinions about taking part in research studies involving the testing of new medicines. These questions discuss the methods that were described in the first part of this information sheet. This is not an examination or a test of your memory or understanding but an attempt to find out what you feel about these kinds of studies and their methods.

I will then give you an information sheet similar to this one and will read it with you. This information sheet is an invitation to participate in an IMAGINARY study where the people who participate will be given either a new medicine for their problem or a dummy medicine. The information sheet will describe the details of the new medicine as well as the details of what people who take part in the research will have to do. This information sheet is very similar to what people would actually receive when they are asked to participate in research on new medicines. However, this invitation is NOT for a real trial that **you** are expected to participate in, or approve as the relative of a patient, but only an exercise to understand what you feel about being invited to take part in such a trial. It will help my study if you can imagine that you were actually being invited to participate in a real study of a new drug.

After I have given you an opportunity for you to ask questions about this imaginary study, I will then check to see if you have understood what the study is about and will

ask you some questions about the methods of this imaginary study and what will be expected of you.

I will then ask you (as a patient) and your relative to decide whether you will agree to participate in the imaginary study and are willing to sign the consent form, though you will NOT be asked to actually sign the form.

If you (as a patient) decide not to take part in this imaginary research study on the new medicine, I will ask you some questions about why you decided not to take part. You are free to state whatever reasons you wish to give as this will help us understand what part of the research made you decide not to take part. If you are the relative of a patient, and decide that the patient should not take part in this imaginary study, I will ask you for your reasons and encourage you to help us understand your reasons for this decision.

If you (as a patient) decide to participate in the imaginary trial, I will then ask you some questions about what made you decide to participate. If you are the relative of a patient, and decide that you feel that that the patient should take part in this imaginary study, I will ask you for your reasons and encourage you to help us understand your reasons for this decision.

If you (as a patient) decide to participate in the imaginary trial, I will then invite you to participate in an additional part of the same trial that requires you give some blood on different occasions and to take part in some special tests. I will again test your understanding of the information given to you about this extension study. You will be asked for permission to take part in these additional parts of the study and your decision and the reasons for your decision will be noted. If you are a relative of the patient, you will also be given information about the additional parts of the study, you understanding assessed, and your opinion on whether your relative should or should not take part in these extensions will be noted along with your reasons. With this my interview will end.

For the next part of my study, I request your permission for my senior, Dr Sumail Dholakia who is a consultant psychiatrist in this hospital, to again interview you regarding your understanding of this research study as well as the imaginary research study using a different set of questions. This interview will take place within 24-48 hours of my interview and should last about half an hour. He will also request you to permit him to record the interview with him using a voice recorder. The questions he will ask will help us understand how well you understood the research study and whether you made your decision with all the required information. This will also help us to decide whether we need to use these questions routinely when we invite people to take part in research.

If you agree to participate in my research study, what will be your responsibilities?

If you agree to take part, all you will be expected to do is take part in the interviews and answer the questions to the best of your ability. No other responsibilities will be expected of you.

Will information from this study be kept confidential?

Yes. Information collected for this study and all your opinions and your answers to the questions will be kept confidential. We will make sure that you will not be identified by name or in any manner that will reveal your identity in any way. Only the people named in this information sheet as the investigators will know who you are and the voice recordings of your interviews will not have your name or identifying details and will only have a code number that will be known only to me.

What are the benefits of taking part in this study?

Since we are not changing or adding to the treatment given in this hospital, taking part in this research study will not directly benefit you. We will also not be providing you with any financial or other compensation for your participation. However, taking part in this study will help you to learn more about how research is done for new medicines. Your taking part in this study may help other patients in the future, as this study will help us to understand how to make research more helpful for the patients who actually take part in research involving new medicines.

What are the possible risks or harms that can happen due to taking part in this study?

We do not believe that taking part in this study can cause any harm to you. If any of the questions are distressing you are free not to answer them. If the interview is distressing, or tiring, please tell me and I shall make sure we stop the interview and hope we can complete it later, if you agree.

Is it possible to withdraw from the study, after I agree to take part?

You do not have to agree to take part in this study. Even if you agree to take part, you are free to take back your consent and discontinue your participation at any time. We will ask you for your reasons for not participating or for deciding to stop talking part after agreeing to do so, but you do not have to give us any reasons, if you do not wish to do so.

Your refusal to participate now or at any time will not upset us or make us displeased with you or change the attitudes of the hospital staff towards you or affect your treatment in any way.

Who is paying us for this research?

None of us are getting any money personally for doing this research. The costs of preparing the paper forms for the interviews and for translating and writing the recorded conversations and for analysis of the results are being paid from money given for this purpose by the Christian Medical College, Vellore.

Can I find out what were the results of your research study?

We hope to publish the results of this study in a medical journal that will present the overall results but will not give the results for any individual person who took part in this study. Any result that is from any person will not be identifiable from the publication report.

If you want to know the results of the study, please leave with us your contact address so that we can send you a summary of the results after we have finished the study. We will not be able to give you your results alone or that of anyone else in this study, apart from the overall study results.

Who can you call if you have questions?

You can call me Dr. Donae George on my mobile 9442555421 or you can call Psychiatry Unit II office: 0416-2284520 during working hours and ask for me by name. You can also call the Psychiatry Unit II Office and ask to speak to Dr. Saumil Dholakia or Dr Prathap Tharyan.

INFORMED CONSENT FORM 1b

Title of the study :

Assessment of attitudes towards participation, willingness to participate, and competence to participate in Randomized Controlled Trials

Name of the investigators and institution:

Dr. Donae George, Dr. Saumil Dholakia, Dr. Prathap Tharyan; Christian Medical College, Vellore

Study Number:

Participant's name:

Date of Birth / Age (in years):

Status: Inpatient/ relative of in-patient

I_____, son/daughter of _____declare that I have read the information sheet in _____ provided to me/ had this information read out to me regarding this study and have clarified any doubts that I had.

I understand that my participation in this study is entirely voluntary and that I am free to withdraw my decision to continue to participate at any time without affecting my medical care / my relative's medical care.

I understand that during this study I will be required to take part in an interview conducted by Dr. Donae that will ask me my opinions about clinical research and discuss taking part in an imaginary study of a new medicine. I understand that this interview may last from half an hour to an hour or more.

I understand that I will be also required to take part in another interview lasting for about half an hour conducted by Dr. Saumil that will ask me additional questions about my understanding about the details of the imaginary study.

I understand that I am expected to cooperate with the interviews and answer the questions asked of me to the best of my ability.

I understand that the interviews will be audio taped but my identity will not be revealed the opinions I express in the interview will not be used for purposes other than those of the study.

I understand that all my opinions and information about me will be kept confidential and that my identity will not be revealed in any information released to third parties or if published in medical journals.

I understand that participating in this study will not affect my clinical care nor will it benefit me directly. I also understand that I will not be given any compensation for my participation.

I also understand that the study staff and, if needed, the institutional ethics committee members, will not need my permission to look at my health records /my relative's health records even if I withdraw from the trial.

I consent to participate in this study and in the interviews conducted by Dr. Donae.

I consent to participate in the interviews to be conducted by Dr. Saumil.

I consent to the interviews being audio-recorded.

Name:

Signature:

Date:

Name of witness

Relation to participant:

Date:

Key relatives consent:

I, _____, relative of _____, have read the information provided and clarified my doubts. I consent to my relative participating in the trial as described in the information sheet.

I consent to participate in this study and to the conditions described in the information sheet.

Name:

Signature:

Date:

Relation to participant:

Appendix 2

Data Extraction Sheet

Patient Identification Details

Date of assessment: date of admission: number of days since admission:

Type of admission: voluntary/involuntary

Serial No: Psych Unit: Room category: Hospital No:

Patient Name: age: sex: education:

Literacy status: identify/understand/interpret/create/communicate/compute written and printed material: (tick as applicable)

Occupation: language: concession for treatment if any:

Name of key relative:

Relationship to the patient:

Past history of psychiatric illness in key relative and details if any:

Current evidence of psychiatric illness on clinical interview in key relative(yes/no):

Current medication in key relative (yes/no), if yes details:

Disease profile:

Diagnosis (ICD 10 code): duration of illness (months):

Duration of current exacerbation (months):

Presence of active psychotic symptoms (delusions/hallucinations) in past 24 hrs: present/probable/unclear/absent:

Insight (grade 1-6):

Current medication:

Documented presence of treatment non-response in the past: (yes/no)

Present CGI score:

1. Severity of illness

Considering your total clinical experience with this particular population, how mentally ill is the patient at this time?

0 = Not assessed

1 = Normal—not at all ill, symptoms of disorder not present past seven days

2 = Borderline mentally ill—subtle or suspected pathology

3 = Mildly ill—clearly established symptoms with minimal, if any, distress or difficulty in social and occupational function

4 = Moderately ill—overt symptoms causing noticeable, but modest, functional impairment or distress; symptom level may warrant medication

5 = Markedly ill—intrusive symptoms that distinctly impair social/occupational function or cause intrusive levels of distress

6 = Severely ill—disruptive pathology, behavior and function are frequently influenced by symptoms, may require assistance from others

7 = Among the most extremely ill patients—pathology drastically interferes in many life functions; may be hospitalized

Appendix 3

Attitudes to Research Questionnaire

Information about this questionnaire:

In the information provided to you earlier, I told you about the kind of research that is done to be sure a new medicine actually can result in benefit for people with specific medical or psychiatric conditions. I told you that in such studies (called RCTs or clinical trials), the patient and the doctor do not decide who is given the new medicine and who is not given a dummy medicine that looks identical to the new medicine, but that this is decided by a method similar to a lottery system. This is different from what you normally expect when you come to a hospital for treatment.

People have varied views, opinion and beliefs regarding research and taking part in RCTs. These influence their choices of accepting/rejecting participation in them. We would like to know your views and request you to choose the single response to each question that most closely reflects what you feel about each question. There are no right or wrong answers as your views are important. For each choice you make we will request you to give us reasons as to why you made that choice. We will be recording your answers so that we can accurately understand your opinions.

Kindly circle the most appropriate response:

1) It is necessary to test new drugs scientifically before using them in clinical practice?
   Strongly agree----agree---------don't know------disagree------strongly disagree.

2) Patients take part in research trials because they expect to get personal health care and health benefits.
   Strongly agree----agree------don't know--------disagree-------strongly disagree.

3) Doctors do research trials with a motive to "experiment" a new treatment option on the patient.
   Strongly agree---agree------don't know---- disagree------- strongly disagree.

4) Patients taking part in research trials do it mainly because they expect to get monetary benefits.
   Strongly agree-----agree----don't know-----disagree------strongly disagree.

5) Doctors do research trials as a way to promote their own careers.
   Strongly agree------agree----don't know-----disagree------strongly disagree.

6) Patients who participate in research do it because they believe that their participation will help in reducing human suffering as a whole.
   Strongly agree-----agree----don't know-------disagree------strongly disagree.

7) Doctors do research trial with the sole aim to help their patients.
   Strongly agree------agree-----don't know-------disagree-----strongly disagree.

8) Patients find it very difficult to trust the motives of the doctors and the organization doing a clinical trial.
   Strongly agree-----agree------don't know-------disagree-------strongly disagree.

9) Research trials of this nature are time consuming and interfere with the doctor's work of looking after patients.
   Strongly agree----agree------don't know--------disagree------strongly disagree.

10) Research trials of this nature do not fully address patients concerns about whether the drug is effective or safe
    Strongly agree------agree------don't know-------disagree------strongly disagree.

11) For patients, faith in the doctor and the institution are the most important motivating factors behind deciding to take part in a clinical trial.
    Strongly agree-----agree------don't know-----disagree------strongly disagree.

12) The information provided in consent forms are very difficult for patients to understand.
    Strongly agree-----agree-------don't know-------disagree------strongly disagree.

13) The decision to participate or not to participate in in a clinical trial is a family decision and cannot be taken by the patient alone.
    Strongly agree------agree-------don't know-------disagree-----strongly disagree.

14) Taking part in clinical trials usually results in others finding out confidential information about patients
    Strongly agree-----agree------don't know------disagree--------strongly disagree.

15) The methods of RCTs where patients and doctors do not have a choice in which treatment the patient is given is justified in order to be sure the new drug actually works.
    Strongly agree------agree------don't know-------disagree---------strongly disagree.

16) In RCTs, giving half the patients a dummy tablet that looks identical to a new medicine is not justified even if it is good way to do research
    Strongly agree------agree------don't know-------disagree---------strongly disagree.

17) If patients sign a consent form to take part in a RCT where they or the doctor have no choice in the treatment given and do not know if they are on treatment or a dummy tablet, then it is justified to use such methods.
    Strongly agree------agree------don't know-------disagree---------strongly disagree.

18) Involving patients in understanding more about research and helping to design how research should be done is not necessary.
Strongly agree------agree------don't know-------disagree---------strongly disagree.

19) Since I enjoy the benefits of medicines because other people have taken part in research to prove the medicine works, I believe it is the duty of everyone to also take part in such research, if requested.
Strongly agree------agree------don't know-------disagree---------strongly disagree.

20) If I were invited to take part in a clinical trial of a new medicine compared against a dummy tablet, I will most probably agree to take part in this study
Strongly agree------agree------don't know-------disagree---------strongly disagree.

Appendix 4a

Christian Medical College, Vellore

Department of Psychiatry

A randomized controlled trial comparing drug GVV278 with placebo in to reduce stress-related symptoms in people with psychiatric disorders

Information sheet

Invitation to participate in a randomized controlled trial (RCT)

You are being requested to participate in a study to see if a new medicine called GVV278 can help reduce some of the symptoms of the psychiatric condition that you are admitted here for. This study aims to recruit a minimum of 30 patients from this hospital and is also being conducted in other institutions in India and other countries to achieve a target sample size of 800 participants.

[This study has been approved by the Institutional Review Board (Research and Ethics Committees) of the Christian Medical College, Vellore, as a hypothetical study (imaginary study) done as part of another study evaluating the attitudes of patients and participants on participating in clinical trials]

What is the new medicine supposed to do?

GVV278 has been shown in laboratory research to reverse the effects of stress in laboratory animals. It has been tried in research involving 20 people with no psychological problems who took GVV278 for over one year and experienced no troubling side effects at doses of 10 mg, 20 mg, and 30 mg taken orally in the morning after breakfast. Analysis of the effects of the different doses on psychological test performance of these people indicates that the 20 mg per day dose is the dose that is most likely to help reduce symptoms of stress.

In one clinical trial involving 25 people from Brazil with different psychiatric conditions but who were also experiencing symptoms related to stress such as tiredness, headaches, sleep disturbance, and irritability, GVV278 was shown to be useful in reducing symptoms and reducing scores on psychiatric tests for symptoms of the underlying disorder. However, because this study involved only a small number of people and because GVV278 was not compared with a dummy tablet, doctors are not certain if the improvement seen in those given GVV278 in addition to their usual treatment was due to GVV278 or due to their usual treatment or due to chance.

There are also other drugs that can help in your problem and you may already be taking medication for your problem that is prescribed by your doctor.

How does GVV278 act to help reduce stress related symptoms?

It is not entirely clear how this drug acts as there are many chemical changes that take place in the brain that seem to work together to result in the effects that GVV 278 has.

Does GVV278 have any side effects?

Some people on GVV278 have experienced some side effects such as headache, feeling anxious, feeling like vomiting, loose motion and stomach discomfort, but these were usually mild and temporary. GVV278 does not cause addiction or any problems when it is stopped suddenly. It may cause mild increases in blood pressure but these are usually not serious. It is not known to cause any problems to the heart.

How is this research study designed to prove the effects of GVV278?

This study will use a research design called a randomized controlled trial (or RCT) where every patient who is eligible and who consent to participate will be given an identical looking tablet to take after breakfast daily for 8 weeks. Half the participants in the trial will actually get GVV278 for the 8 weeks and the other half will get an identical looking tablet that does not contain GVV278 but contains only a small amount of sucrose (like sugar) that is unlikely to have any effect in the person taking it. The choice of who gets GVV278 or the dummy tablet has been decided by a computer that provided a code to the pharmacist of the company sponsoring this study in Switzerland. They have prepared serially-numbered containers containing one week's supply of GVV or the dummy tablet, according to the randomization code. The doctors in this hospital conducting the study do not have access to this code and do not know what is in any of the tablets. This information is only known to the company sponsoring the trial. The doctors in this hospital are only provided with the serially numbered, coded medicine containers that have identical looking medicines for 8 weeks of treatment for the patients who will be recruited to the trial from this hospital.

Since the selection of who gets which tablet will be decided by the code, we expect that this will result into equal selection of people in both groups especially with relation to severity of symptoms.If this is not done, this may result in more sick people being selected to take GVV278 or the dummy tablet and we will not be sure if any difference in the results were due to any of the tablets or due to that fact that there were more sick people who got one of the tablets. We expect that by this method all people irrespective of the severity of symptoms will get an equal chance to get GVV278 or the dummy tablet

In addition, since both tablets are identical, the doctors who will decide if GVV278 or the dummy tablet causes more improvement, and patients who are taking part in the study will not be influenced by what they expect either tablet to do with regard to improvement in symptoms or in causing side effects, since nobody in this hospital knows who is taking GVV278 or the dummy tablet. Every week for the first month and at the end of 8 weeks, all participants in the study will be assessed for improvement in symptoms or the presence of side effects. Once these assessments are over the code will be opened and then statistical tests will be done to see if the differences in the results shows that GVV was better than the dummy tablet in improving symptoms and if there were more side effects with GVV or with the dummy tablet.

This method is the best method to be sure of the effects of GVV on stress-related symptoms in people with psychiatric disorders.

What will be expected of you if you agree to take part in this study?

Once you agree to take part in this study, and have signed the informed consent form, your regular treatment will be changed during the period of this study and you will be given only a mild sedative for week, if you have sleep disturbance. This is to be sure that all your previous medicines are no longer in your body. At the end of one week, I will assess you for your symptoms in a clinical interview and if you do not have enough symptoms your participation in the study will end and you will be requested to discuss with your treating team about whether you should continue on your usual medicines.

If you still have troubling symptoms after a week, you will be asked to take one tablet every morning after breakfast for 8 weeks. This tablet will have either GVV or the dummy tablet but neither you nor I will know what is in the tablet you will be given. I will see you every day for the first four weeks during which you are expected to stay in the hospital as an in-patient. I will ask you for any side-effects due to the medicine you are taking.

During this time you may experience worsening of your condition, including increased symptoms such as agitation, restlessness or decreased sleep. I will carefully monitor your condition and report it to your treating doctors as well. If your symptoms worsen and make you uncomfortable, you can withdraw from the study. You can do this at any time during the stud*y,* and you will be put back on your previous medicine. I will also ask you questions daily about your sleep, activities, and how you feel, in addition to asking you about any side effects. Your weight and blood pressure will also be recorded daily for as long as you are in hospital. No additional procedures or blood tests will be conducted routinely for this study.

If at any time you experience any problems, you will be expected to report this to me, or the nurses or to your doctor. If I or the other doctors in this study or your treating doctor feel that you are not showing satisfactory improvement or are getting worse on the tablet you are taking, we shall withdraw you from the study and you will be put back on your previous medicine.

At the end of four weeks, you will be discharged if you are at least 50% better than when you started the new tablet. You will be contacted by telephone once a week by me or one of the doctors in this study who will ask you about any side effects that you are experiencing and rate your improvement by asking you questions about your sleep, appetite, mood, energy, and daily routine.

At the end of 8 weeks, you will be expected to return for a final visit for the study where you will have all the assessments that were done on you at the start repeated and your weight and blood pressure monitored.

If you are not at least 50% better by the end of four weeks, you will be expected to stay on as an inpatient and assessed every week. If you achieve 50% improvement at any of the weekly assessment, you will be discharged and followed up as described above.

Can you withdraw from this study after it starts?

Your participation in this study is entirely voluntary and you are also free to decide to withdraw permission to participate in this study, for any reason. If you do so, this will not affect your usual treatment at this hospital in any way. In addition, if you experience any serious side effects or your condition worsens, the study tablets will be stopped and you may be given additional treatment.

What will happen if you develop any study related injury?

We do not expect any serious injury to happen to you but if you do develop any side effects or problems due to the study, these will be treated at no cost to you. We are unable to provide any monetary compensation, however.

Will you have to pay for the study tablets?

Both GVV278 and the dummy tablets will be given free for a total period of 8 weeks. Your hospital charges for these eight weeks will also be made free, but you will have to pay for your food, if this is the usual arrangement you have with your treating doctor. In addition, you will also be reimbursed 250 Rs for any outpatient visit you make for the purposes of this study from the time you were discharged till the end of the study. If the cost you incur is more, this additional amount will also be reimbursed if you provide us the receipts or tickets. We will also reimburse 250 Rs (or any additional amount supported by tickets or receipts) for one family member to accompany you on these visits.

What happens after the study is over?

You may or may not benefit from the study medicine that you are given. Once the study is over, if the tablet you were given is GVV278 and if it has helped you and you wish to continue, then your doctor may prescribe it for you. Otherwise, your treating doctor will help you decide on the best treatment for you to continue after the study is over. If you were given the dummy tablet and GVV278 has helped the people in this study who took it, then your doctor will give you the choice of taking GVV278. However, this will not be part of the study and you may have to pay for it. It may also take up to a year after the study for the government to approve GVV278 for sale in India as the results of treating people from all over India who take part in this trial will have to be analyzed. We may not be able to assure you a ready supply of GVV278 from the company till then, although the company has promised to give us stocks of the medicine.

Will your personal details be kept confidential?

The results of this study will be published in a medical journal but you will not be identified by name in any publication or presentation of results. However, your medical notes may be reviewed by people associated with the study, without your additional permission, should you decide to participate in this study.

Who can you call if you have questions?

You can call me Dr. Donae George on my mobile 9442555421 at any time, or you can call Psychiatry Unit II office: 0416-2284520 during working hours and ask for me by name. You can also call the Psychiatry Unit II Office and ask to speak to Dr. Saumil Dholakia or Dr Prathap Tharyan.

INFORMED CONSENT FORM 4a

Title of the study:

A randomized controlled trial comparing drug GVV278 with placebo in to reduce stress-related symptoms in people with psychiatric disorders

Name of the investigators and institution:

Dr. Donae George, Dr. Saumil Dholakia, Dr. Prathap Tharyan; Christian Medical College, Vellore

Study Number:

Participant's name:

Date of Birth / Age (in years):

I_____, son/daughter of _____ declare that I have read the information sheet in _____ provided to me/ had this information read out to me regarding this study and have clarified any doubts that I had.

In understand that I am being invited to participate in a research study that involves changing my current medicines, and being on no medicines for a week, except a mild sedative if needed. I understand that I will be invited to take the study medicines only if I continue to have troubling symptoms after a week of stopping my current medicines.

I understand that my participation in this study is entirely voluntary and that I am free to withdraw my decision to continue to participate at any time without affecting my medical care or my legal rights.

I understand that during this study I will be required to take remain as an inpatient for 4 weeks at least and take one tablet every day for a total of 8 weeks.

I understand that neither I nor any of the doctors in this hospital will have any choice in whether I am given GVV278 or a dummy tablet that looks identical to GVV278. This selection will occur by chance, as in a lottery, and I will have an equal chance of getting GVV278 or the dummy tablet.

I understand that I will also have to cooperate with assessments for this study as explained to me in the information sheet.

I understand that I may or may not benefit by participation in this trial and that if I develop any study related injury, I will not receive any compensation, though I will be not be charged for the treatment of study related injury.

I understand that the study medicines will be provided free of charge for 8 weeks and that if I chose to continue any of the study medicines after 8 weeks, I shall have to bear the costs. I also understand that a regular supply of the study medicine cannot be assured.

I understand that all information about me will be kept confidential and that my identity will not be revealed in any information released to third parties or if published in medical journals.

I also understand that the study staff and, if needed, the institutional ethics committee members, will not need my permission to look at my health records /my relative's health records even if I withdraw from the trial.

I consent to participate in this study and to the conditions described in the information sheet.

Name:

Signature:

Date:

Name of witness

Relation to participant:

Date:

Key relatives consent:

I, _____, relative of _____, have read the information provided and clarified my doubts. I consent to my relative participating in the trial as described in the information sheet.

I consent to participate in this study and to the conditions described in the information sheet.

Name:

Signature:

Date:

Relation to participant:

Appendix 4b

Comprehension of information for the Hypothetical RCT on GVV278 versus placebo

I shall ask you some questions to assess whether you have understood essential details about the RCT you were invited to participate in. If you are unsure of the answer to any of the questions, I shall clarify this information for you.

I shall read out the questions loud and I will record your answers. This interview is also being recorded by voice recorder to make sure your replies are correctly understood.

1. The new drug GVV278 has been found in previous research to be better than currently used medicines in treating symptoms of psychiatric conditions.
True / False / Unsure / Other

2. If you agree to take part in this study, your treating doctor or I will decide whether you will get GV278 or the dummy tablet
True / False / Unsure / Other

3. If you agree to take part in this study, you will be given the study medicine as well as you usual medicines that you are now taking.
True / False / Unsure / Other

4. If you agree to take part in the study, you will be able to find out what medicine you have been given by asking one of the doctors or nurses in this hospital or the pharmacist at this hospital.
True / False / Unsure / Other

5. If you agree to take part in this study, you will be expected to take the study medicine for period of 4 weeks.
True / False / Unsure / Other

6. If you agree to take part in this study, you are likely to feel better whatever the medicine you are given.
True / False / Unsure / Other

7. If you agree to take part in this study, you are not likely to feel worse in any way, if you are actually given the new medicine GVV278.
True / False / Unsure / Other

8. If you agree to take part in this study, you will be given free food and 200 Rs per day
True / False / Unsure / Other

9. If you agree to take part in this study, you will have blood tests done every week while you are in hospital
True / False / Unsure / Other

10. If you agree to take part in this study, and if you are given the dummy tablet, you are likely to feel worse than if you were given the new medicine GVV278.
True / False / Unsure / Other

Thank you for your time and for answering my questions. I will now discuss your answers with you.

Appendix 4c

Clarifying questions and probes to assess barriers and facilitators to participation in a hypothetical RCT

1. Willingness to participate in the RCT of GVV278 versus placebo

Now that you have understood the information provided about the RCT comparing the new medicine GVV278, how likely is it that you will be willing to sign the informed consent document to participate in the study?

Most unlikely to participate	Probably unlikely to participate	Unsure	Probably likely to participate	Very likely to

2. Open ended questions to clarify the choice

What are the reasons for you to make the choice that you did?

Probes: Were there any elements in the information provided about the study that influenced your choice?

Specific probes: Did the fact that your usual medicines would be withdrawn give you concerns?

Did the fact that you would not have any choice in the drug you received cause concern?

Did the fact that your doctor would not have a choice in what medicine you got cause concern?

Did the fact that a dummy tablet was used cause concern?

Were there any other aspects of this trial that caused concern?

If this had been a real trial, would you have changed your choice?

Do you think trials like this should be done?

Do you think that if your treating doctor recommended that you should take part in the trial, you would be more likely to agree to participate?

Appendix 4d

Extension 1 to the hypothetical RCT: information sheet and consent form

Christian Medical College, Vellore

Department of Psychiatry

A randomized controlled trial comparing drug GVV278 with placebo in to reduce stress-related symptoms in people with psychiatric disorders-study extension 1

The detailed information regarding the new medicine GVV278 was discussed with you during the first part of the study. Do you want me to repeat any of the information? In case the details are not clear to you, I would like to repeat it as follows. If it is clear to you, than we may move on to understanding what will be expected out of you if you decide to take part in this study extension.

How is this research study designed to prove the effects of GVV278?

This study will use a research design called a randomized controlled trial (or RCT) where every patient who fulfills the criteria for inclusion in the study and who consent to participate will be given an identical looking tablet to take after breakfast daily for 8 weeks. Half the participants in the trial will actually get GVV278 for the 8 weeks and the other half will get an identical looking tablet that does not contain GVV278 but contains only a small amount of sucrose (like sugar) that is unlikely to have any effect in the person taking it. The choice of who gets GVV278 or the dummy tablet has been decided by a computer that provided a code to the pharmacist of the company sponsoring this study in Switzerland who prepared serially-numbered containers containing one week's supply of GVV or the dummy tablet, according to the randomization code. The doctors in this hospital conducting the study do not have access to this code and do not know what is in any of the tablets. This information is only known to the company sponsoring the trial. The doctors in this hospital are only provided with the serially numbered, coded medicine containers that have identical looking medicines for 8 weeks of treatment for the patients who will be recruited to the trial from this hospital.

Since the selection of who gets which tablet will be decided by the code, this will prevent anyone selecting sicker (people with more severe symptoms) to take either GVV27 or the dummy tablet for any reason. If this is not done, this may result in more sick people being selected to take GVV278 or the dummy tablet and we will not be sure if any difference in the results were due to any of the tablets or due to that fact that there were more sick people who got one of the tablets. We expect that by this method there will be equal numbers of people who have more severe

symptoms and those who have less severe symptoms who will get GVV278 and the dummy tablet

In addition, since both tablets are identical, the doctors who will decide if GVV278 or the dummy tablet causes more improvement, and patients in the study who are taking the tablets and who will report to the doctors about any benefits or side effects of the treatment, will not be influenced by what they expect either tablet to do with regard to improvement in symptoms or in causing side effects, since nobody in this hospital knows who is taking GVV278 or the dummy tablet. Every week for the first month and at the end of 8 weeks, all participants in the study will be assessed for improvement in symptoms or the presence of side effects. Once these assessments are over the code will be opened and then statistical tests will be done to see if the differences in the results shows that GVV was better than the dummy tablet in improving symptoms and if there were more side effects with GVV or with the dummy tablet.

This method is the best method to be sure of the effects of GVV on stress-related symptoms in people with psychiatric disorders.

What will be expected of you if you agree to take part in this study?

Once you agree to take part in this study, and have signed the informed consent form, your regular treatment will continue as prescribed by your treating doctor during the period of this study and you will not be expected to make any changes to these medicines for the 8 weeks of the trial.

At the start of the study, you will be asked to take one tablet every morning after breakfast for 8 weeks. This tablet will have either GVV or the dummy tablet but neither you nor I will know what is in the tablet you will be given. I will see you every day for the first four weeks during which you are expected to stay in the hospital as an in-patient. I will ask you for any side-effects due to the medicine you are taking.

During this time you may experience worsening of your condition although we are uncertain whether this will occur of what symptoms might be caused. I will carefully monitor your condition and report it to your treating doctors as well. If your symptoms worsen and make you uncomfortable, you can withdraw from the study. You can do this at any time during the stud*y,* and you will be put back on your previous medicine. I will also ask you questions daily about your sleep, activities, and how you feel, in addition to asking you about any side effects. Your weight and blood pressure will also be recorded daily for as long as you are in hospital.

Since we wish to make sure that the combination of GV278 and your usual medicines will not cause any problems, if you agree to take part in this extension study, we will perform blood tests to check your liver functions, kidney functions etc. at the start of the study and weekly for the first four weeks and at the end of 8 weeks. We will

withdraw about 10 ml of blood each time. Any remaining blood after the tests will be discarded. In addition, we will perform an EEG to assess your brain electrical activity and an ECG to assess your heart's electrical activity at the beginning and the end of the study. The EEG and the ECG will be done in the laboratories of the main CMC Hospital by special appointment and will be painless procedures. We will provide more information about these procedures once you agree to participate.

If at any time you experience any problems, you will be expected to report this to me, or the nurses or to your doctor. If I or the other doctors in this study or your treating doctor feel that you are not showing satisfactory improvement or are getting worse on the tablet you are taking, we shall withdraw you from the study and you will be put back on your previous medicine.

At the end of four weeks, you will be discharged if you are at least 50% better than when you started the new tablet. You will be contacted by telephone once a week by me or one of the doctors in this study who will ask you about any side effects that you are experiencing and rate your improvement by asking you questions about your sleep, appetite, mood, energy, and daily routine.

At the end of 8 weeks, you will be expected to return for a final visit for the study where you will have all the assessments that were done on you at the start repeated and your weight and blood pressure monitored.

If you are not at least 50% better by the end of four weeks, you will be expected to stay on as an inpatient and assessed every week. If you achieve 50% improvement at any of the weekly assessment, you will be discharged and followed up as described above.

Can you withdraw from this study after it starts?

Your participation in this study is entirely voluntary and you are also free to decide to withdraw permission to participate in this study, for any reason. If you do so, this will not affect your usual treatment at this hospital in any way. In addition, if you experience any serious side effects or your condition worsens, the study tablets will be stopped and you may be given additional treatment.

What will happen if you develop any study related injury?

We do not expect any serious injury to happen to you but if you do develop any side effects or problems due to the study, these will be treated at no cost to you. We are unable to provide any monetary compensation, however.

Will you have to pay for the study tablets?

Both GVV278 and the dummy tablets will be given free for a total period of 8 weeks. Your hospital charges for these eight weeks will also be made free, but you will have to pay for your food, if this is the usual arrangement you have with your treating

doctor. In addition, whatever medicine you are being prescribed at the start of the study will also be paid for and you will not have to pay for them. All the investigations associated with the study will also be done free of cost.

You will also be reimbursed 250 Rs for any outpatient visit you make for the purposes of this study from the time you were discharged till the end of the study. If the cost you incur is more, this additional amount will also be reimbursed if you provide us the receipts or tickets. We will also reimburse 250 Rs (or any additional amount supported by tickets or receipts) for one family member to accompany you on these visits.

What happens after the study is over?

You may or may not benefit from the study medicine that you are given. Once the study is over, if the tablet you were given is GVV278 and if it has helped you and you wish to continue, then your doctor may prescribe it for you. Otherwise, your treating doctor will help you decide on the best treatment for you to continue after the study is over. In all cases once the study is over, the decision to continue your medicine will be made by your treating doctor in collaboration with you. If you were given the dummy tablet and GVV278 has helped the people in this study who took it, then your doctor will give you the choice of taking GVV278. However, this will not be part of the study and you may have to pay for it. It may also take up to a year after the study for the government to approve GVV278 for sale in India as the results of treating people from all over India who take part in this trial will have to be analyzed. We may not be able to assure you a ready supply of GVV278 from the company till then, although the company has promised to give us stocks of the medicine.

Will your personal details be kept confidential?

The results of this study will be published in a medical journal but you will not be identified by name in any publication or presentation of results. However, your medical notes may be reviewed by people associated with the study, without your additional permission, should you decide to participate in this study.

Who can you call if you have questions?

You can call me Dr. Donae George on my mobile 9442555421 at any time, or you can call Psychiatry Unit II office: 0416-2284520 during working hours and ask for me by name. You can also call the Psychiatry Unit II Office and ask to speak to Dr. Saumil Dholakia or Dr Prathap Tharyan.

INFORMED CONSENT FORM 4d

Title of the study:

A randomized controlled trial comparing drug GVV278 with placebo in to reduce stress-related symptoms in people with psychiatric disorders-Study extension 1

Name of the investigators and institution:

Dr. Donae George, Dr. Saumil Dholakia, Dr. Prathap Tharyan; Christian Medical College, Vellore

Study Number:

Participant's name:

Date of Birth / Age (in years):

I_____, son/daughter of _____ declare that I have read the information sheet in _____ provided to me/ had this information read out to me regarding this study and have clarified any doubts that I had.

In understand that I am being invited to participate in a research study that involves continuing on my current medicines and adding a new medicine GVV278 or a dummy tablet for a period of 8 weeks.

I understand that my participation in this study is entirely voluntary and that I am free to withdraw my decision to continue to participate at any time without affecting my medical care or my legal rights.

I understand that during this study I will be required to take remain as an inpatient for 4 weeks at least and take one tablet every day for a total of 8 weeks.

I understand that neither I nor any of the doctors in this hospital will have any choice in whether I am given GVV278 or a dummy tablet that looks identical to GVV278. This selection will occur by chance, as in a lottery, and I will have an equal chance of getting GVV278 or the dummy tablet.

I understand that I will also have to cooperate with assessments for this study as explained to me in the information sheet. These assessments include blood tests and EEG and ECG tests as described in the information sheet.

I understand that I may or may not benefit by participation in this trial and that if I develop any study related injury, I will not receive any compensation, though I will be not be charged for the treatment of study related injury.

I understand that the study medicines and my regular medicines will be provided free of charge for 8 weeks and that if I chose to continue any of the medicines after 8 weeks, I shall have to bear the costs, or discuss this with my treating doctor. I also understand that a regular supply of the study medicine cannot be assured.

I understand that all information about me will be kept confidential and that my identity will not be revealed in any information released to third parties or if published in medical journals.

I also understand that the study staff and, if needed, the institutional ethics committee members, will not need my permission to look at my health records even if I withdraw from the trial.

I consent to participate in this study and to the conditions described in the information sheet.

Name:

Signature:

Date:

Name of witness

Relation to participant:

Date:

Key relatives consent:

I, _____, relative of _____, have read the information provided and clarified my doubts. I consent to my relative participating in the trial as described in the information sheet.

I consent to participate in this study and to the conditions described in the information sheet.

Name:

Signature:

Date:

Relation to participant:

Appendix 4e

Comprehension of information for the Hypothetical RCT on GVV278 versus placebo-extension 1

I shall ask you some questions to assess whether you have understood essential details about the RCT you were invited to participate in. If you are unsure of the answer to any of the questions, I shall clarify this information for you.

I shall read out the questions loud and I will record your answers. This interview is also being recorded by voice recorder to make sure your replies are correctly understood.

1. The new drug GVV278 has been found in previous research to safe when given along with your currently used medicines in treating symptoms of psychiatric conditions.
   True / False / Unsure / Other

2. If you agree to take part in this study, you will be given the study medicine as well as you usual medicines that you are now taking.
   True / False / Unsure / Other

3. If you agree to take part in this study, you are not likely to feel worse in any way, if you are actually given the new medicine GVV278.
   True / False / Unsure / Other

4. If you agree to take part in this study, you will not have to pay for your usual medicines for the period of the study.
   True / False / Unsure / Other

5. If you agree to take part in this study, you will have an EEG and an ECG done every week while you are in hospital
   True / False / Unsure / Other

Thank you for your time and for answering my questions. I will now discuss your answers with you.

Appendix 4 f

Clarifying questions and probes to assess barriers and facilitators to participation in a hypothetical RCT- extension 1

1. Willingness to participate in the RCT of GVV278 versus placebo- extension 1

Now that you have understood the information provided about the RCT comparing the new medicine GVV278, in this extension study how likely is it that you will be willing to sign the informed consent document to participate in the study?

Most unlikely to participate- probably unlikely—unsure---probably likely--- most likely to participate

2. Open ended questions to clarify the choice

What are the reasons for you to make the choice that you did?

Probes: Were there any elements in the information provided about the study that influenced your choice?

Were there any elements in the information not provided about the study that influenced your choice?

Specific probes:

Did the fact that your usual medicines would be continued influence your decision?

Did the fact that you would have to undergo blood tests cause concern?

Did the fact that you would have to undergo an ECG cause concern?

Did the fact that you would have to have an EEG cause concern?

Were there any other aspects of this trial that caused concern?

If this had been a real trial, would you have changed your choice?

Would you prefer to participate in this extension trial or the previous trial?

Do you think patients and relatives should be involved in helping to design research studies?

Appendix 5

A randomized trial comparing drug GVV278 with placebo to reduce stress related symptoms in people with psychiatric disorders.

MacCAT-CR interview form:

The purpose of our discussion is to know your understanding of imaginary randomized control trial with drug GVV278 (and its extension if applicable) that you have been invited to join. Please do not hesitate to ask any questions as the interview proceeds.

Understanding section:

(Question 1 is a modified question as PI has already gone through the details of project in the information sheet; hence only some details are repeated)

1) Dr. Donae has discussed with about the imaginary research project with drug GVV278 to reduce stress. The project will last for 8 weeks for which you would be staying as inpatient. Your previous medications will be stopped. You would be assessed daily about your sleep, activities and your feelings. Your weight and blood pressure would be daily monitored. You would be asked daily about any side effects.

Question:

Do you have any questions about what i just said/what has been told to you by Dr. Donae?

Can you tell your understanding of what i just said?

Probe: (if the subject fails to respond spontaneously)

- What is the purpose of the research project i described to you?
- How long will the research project last?
- What sort of things will be done with people who agree to take part in the study?
- What else would be done with people who agree to be in the study?

2) it is important that you understand that the project in which you have been asked to take part is a research project and not a part of your treatment. That means that the main purpose is to help doctors decide whether the drug GVV278 can help some people with stress.

Question:

Do you have any questions about what I just said?

Can you tell your understanding of what I just said?

Probe:

- What is the main purpose of what the doctors are trying to do in this study?

3) Because this is a research project and not ordinary treatment, the doctors will be doing things that they would not do in ordinary hospitals or clinics, like those where you may have been treated before. For example out of all the people who agree to take part in this study' some people in this project will get GVV278 but others will get a dummy pill (called a placebo). The pill will not have any medicine in it. Whether they get GVV278 or the dummy pill will be decided by chance. Neither the doctors nor the subjects will know whether they are getting the new medication or the dummy pill. All these things are done to see whether GVV278 is better than no medication at all.

Question:

Do you have any questions about what I just said?

Can you tell your understanding of what I just said?

Probe:

- Will all people in the project get the new medicine?
- How will it be determined what kinds of pills each of the people in the project will receive?
- Who will know which kind of pill is received by which people?

4) There are several benefits that could result if people agree to be in this project. One of the most important benefit is that the doctors would come to know whether the GVV278 really does work with people who have stress related symptoms in people with psychiatric disorders. Secondly, for people in the project who actually get GVV278 will be able to find out whether or not it works for them.

Question:

Do you have any questions about what I just said?

Can you tell your understanding of what I just said?

Probe:

- What might doctors learn about the treatment of stress related symptoms in people with psychiatric disorder s if people decide to take part in this research project?
- In what way might people benefit by volunteering to take part in this study?

5) There are also several risks and discomforts to which people in this study might encounter. Firstly, GVV278 can cause mild problems like headache, nausea, stomach discomfort and loose motions. It may also cause a mild increase in blood pressure. Secondly, all people in the study would be interviewed on a daily basis for at least 4 weeks and maximum 8 weeks which might cause some discomfort to participants.

   Question:

   Do you have any questions about what I just said?

   Can you tell your understanding of what I just said?

   Probe:

   - What unpleasant effects can the medication cause in some people?
   - What can cause some discomfort to most people who take part in the study?

6) It is not compulsory to be a part of this project. People who agree to be in this research project can change their minds at any time. If they donot agree to be in this project or if they decide to stop, their usual treatment would be restarted.

   Question:

   Do you have any questions about what I just said?

   Can you tell your understanding of what I just said?

   Probe:

   - What would happen if a person refuses to be in the research project, or decides to stop once it begins?

Appreciation:

7) a) Do you believe that you have been asked to be in this project mainly for your personal benefit?

   b) What makes you say so?

8) a) do you believe that you could get the dummy pill?

b) What makes you say so?

9) a) what do you believe would happen if you were to decide not to be in this study?

b) What makes you say so?

Expressed choice:

10) As you know, you have been invited to participate in this research project to test a drug named GVV278 for treatment of stress in people with psychiatric disorders. What do you think you are more likely to do—would you want to participate or decline the invitation to participate?

Reasoning

11) You think you are more likely to_____ in the study. Tell me what is it that makes you think that this option is better than the other.

12) I told you about some of the possible benefits and risks and discomforts of participating in the research project. The benefits are that those subjects who actually get GVV278 may find out whether it works for them. The risks and discomforts are that GVV278 can cause headache, nausea, stomach discomfort, a mild increase in blood pressure and all people in the study will have to answer a set of questions every day. Can you tell me in what way this would affect your everyday activities if you participate in this research project?

Probe:

- How might benefits or risks and discomfort affect your everyday life?

13) A few minutes ago you told me that you are more likely to favour participating/not participating in the research project. Now that we have discussed everything, what do you want to do?

Logical consistency of choice: interviewer records and explains the presence or absence of logical consistency in subject's choice. If consistant, no probe required. If not, then the inconsistencies be discussed with the subject until the interviewer understands the basis for the real or apparent disparity.

Appendix 5

A randomized trial comparing drug GVV278 with placebo to reduce stress related problems in people with psychiatric disorders-study extension 1

MacCAT-CR interview form:

The purpose of our discussion is to know your understanding of the imaginary randomized control trial with drug GVV278 study extension that you have been invited to join. Please do not hesitate to ask any questions as the interview proceeds.

Understanding section:

1) Dr. Donae has discussed with you about the extension part of the imaginary research project with drug GVV278 to reduce stress. This extension is to know whether people taking other medications for the treatment of psychiatric conditions would have any problems if they also took GVV278. The study is expected to last for 8 weeks. In this extension, your previous medications will be continued. You will be seen every day for the first 4 weeks during which you are expected to stay as inpatient. Blood tests will be performed at the start of the study and weekly for the first four weeks and then at the end of 8 weeks. In addition, an EEG (Electroencephalogram) and an ECG (Electrocardiogram) would be done in laboratories of the main CMC Hospital by special appointment. At the end of 4 weeks, you will be discharged if you are at least 50% better. You will be contacted once a week by telephone to ask you about any side effects and improvement by asking questions about your sleep, appetite, mood, energy and daily routine. at the end of 8 weeks, you will be expected to return for a final visit for the study when all the assessments done at the start of the study will be repeated and your weight and blood pressure monitored.
   If you are not atleast 50% better at the end of four weeks, you will be expected to stay as inpatient and assessed every week.

   Question:
   Do you have any questions about what I just said/what has been told to you by Dr. Donae?

   Can you tell your understanding of what I just said?

   Probe: (if subject fails to respond spontaneously)
   - What is the purpose of the extension research project I described to you?
   - How long will the project last?
   - What sort of things will be done with people who agree to take part in the study?
   - What else would be done with people who agree to be in the study?

2) It is important that you understand that this extension part in which you have been asked to take part is a research project and not a part of your treatment. That means that the main purpose is to help doctors decide what would happen if people taking medications for treatment of psychiatric conditions are given GVV278.
   - Do you have any questions about what I just said?
   - Can you tell your understanding of what I just said?

Probe:

- What is the main purpose of what the doctors are trying to do in this study?

3) Because this is a research project and not ordinary treatment, the doctors will be doing things that they would not do in clinical settings in hospital or clinics. For example, out of all people who agree to take part in this extension, some people will get GVV278 but other will get a dummy pill (called placebo) along with the medications that they are already taking. The dummy pill will not have any medicine in it. Whether you will get GVV278 or the dummy pill will be decided by chance. Neither the doctors nor you will know wether you are getting the new medication or the dummy pill. All these things are done as doctors want to be relatively sure that if at all people experience any problems when they take GVV278 along with other psychiatric medications; than the problems are due to GVV278 and not due to any other reason.

- Do you have any questions about what I just said?
- Can you tell your understanding of what I just said?

Probe:

- Will all people in the extension project get the new medicine?
- How will it be determined who will get what kind of pills?
- Who will know which kind of pills are received by which people?

4) There are several benefits that could result if people agre to be in this project. One of the most important benefit is that doctors would come to know whether GVV278 causes any problems if given with any other psychiatric medications. Secondly, for people who agree to them when taken along with other psychiatric medications. They would also know whether there are any problems when it is taken with other psychiatric medications.

- Do you have any questions about what I just said?
- Can you tell me your understanding of what I just said?

Probe:

- What would be the benefit to doctors if you decide to take part in this extension?
- What way people might benefit if they volunteer to take part in this extension?

5) There are several risks and discomforts which you might encounter if you agree to take part in this project. Firstly, you will be interviewed on a daily basis for atleast 4 weeks and maximum 8 weeks for monitoring of side effects which might be a cause for discomfort. Secondly, you will have to undergo blood tests where 10ml blood will be taken and send for testing at the start of the study and then on a weekly basis. You will also have to undergo painless procedures like EEG and ECG in the main hospital. Thirdly, if you are 50% better and discharged at the end of 4 weeks, then one of us will be contacting you through telephone on a weekly basis. If you are not 50% better, you would be expected to stay as inpatient and be seen on a weekly basis. All tests will be repeated at the end of 8 weeks.

- Do you have any questions about what I just said?

- Can you tell your understanding of what I just said?

Probe:

- What can cause discomfort to most people who take part in the study?

6) It is not compulsory to be a part of this extension. People who agree to be in this project can change their minds at any time. If they do not agree to be in this project or if they decide to stop, their usual treatment will be continued.

- Do you have any questions about what I just said?
- Can you tell your understanding of what I just said?

Probe: what would happen if a person refuses to be in the research project or decides to stop once it begins?

APPRECIATION:

7) a) Do you believe that you have been asked to be in this extension project mainly for your personal benefit?
b) What makes you say so?

8) a) Do you believe that you could get the dummy pill?
b) What makes you say so?

9) a) What do you believe would happen if you were to decide not to be in this study?
b) What makes you say so?

10) As you know you have been invited to participate in this research project to test the effect of drug gvv278 when taken with other psychiatric medications for the treatment of stress. What do you think you are more likely to do—would you want to participate or decline the invitation to participate?

REASONING

11) You think you are more likely to .....in the study. Tell me what is it that makes you think that this option is better than the other.

12) I told you about some of the possible benefits and discomforts of participating in this extension. The benefits are that those people who actually get GVV278 may find out whether there are any problems with it when they take it with other psychiatric conditions. The discomfort is that they will have to undergo blood tests, EEG and ECG as a part of monitoring these effects and would have to answer questions regarding their condition every day. Can you tell me in what way this would affect your everyday activities if you were to participate in this extension?

Probe:

- How might benefits or discomfort affect your everyday life?

13) A few minutes ago you told me that you are more likely to favour participating/not participating in the research project. Now that we have discussed everything, what do you want to do?

Logical consistency of choice: interview records and explains the presence or absence of logical consistency in patient's and their relative's choice. If consistent no probe required. If not then the inconsistences be discussed with the patient until the interviewer understands the basis for the real or apparent disparity.

Appendix 6

MacCAT-CR Record form

Subject:.....

interviewer:.....

Record ID#:.....

Date:.....

Understanding (each item is rated 0-2)

1) Nature of project
   a)_____
   b)_____
   c)_____
   d)_____ subtotal:

2) Primary purpose is research

   Subtotal:

3) Effects on individualized care
   a)_____
   b)_____
   c)_____ subtotal:

4) Benefits and risks/discomforts
   a)_____
   b)_____
   c)_____
   d)_____ subtotal:

5) Ability to withdraw

   Subtotal:

Total UNDERSTANDING SCORE (0-26): [ ]

APPRECIATION: (each item is rated 0-2)

1) Object not personal benefit:_____
2) Possibility of reduced benefit:_____
3) Withdrawal possible:_____

Total APPRECIATION SCORE (0-6): ☐

Reasoning: (each item is rated 0-2)

1) Consequential reasoning:_____
2) Comparative reasoning:_____
3) Generating consequences:_____
4) Logical consistency of choice:_____

Total REASONING SCORE (0-8): ☐

EXPRESSING A CHOICE: (rate 0-2)

_____

Total EXPRESSING A CHOICE SCORE (0-2): ☐

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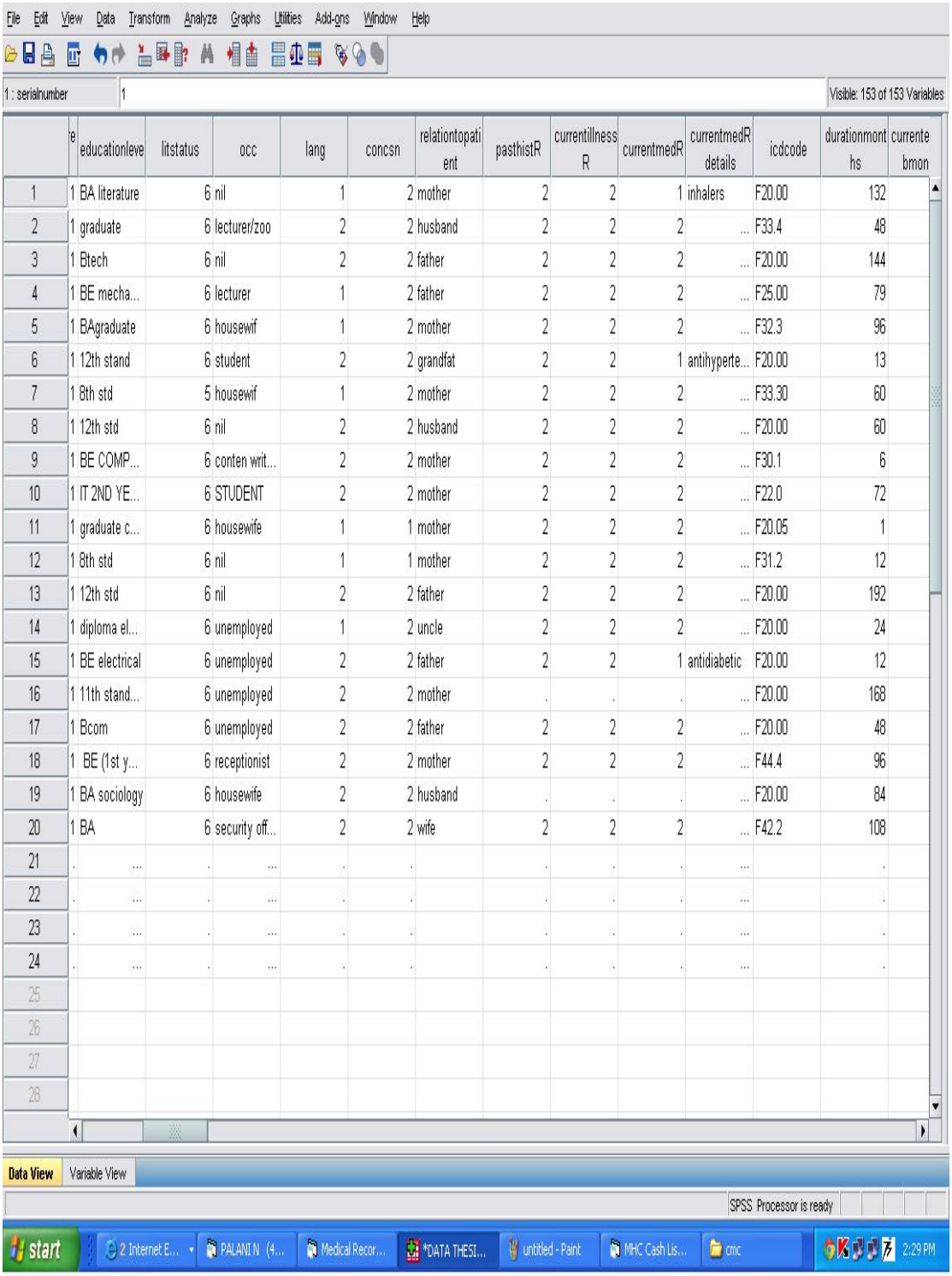

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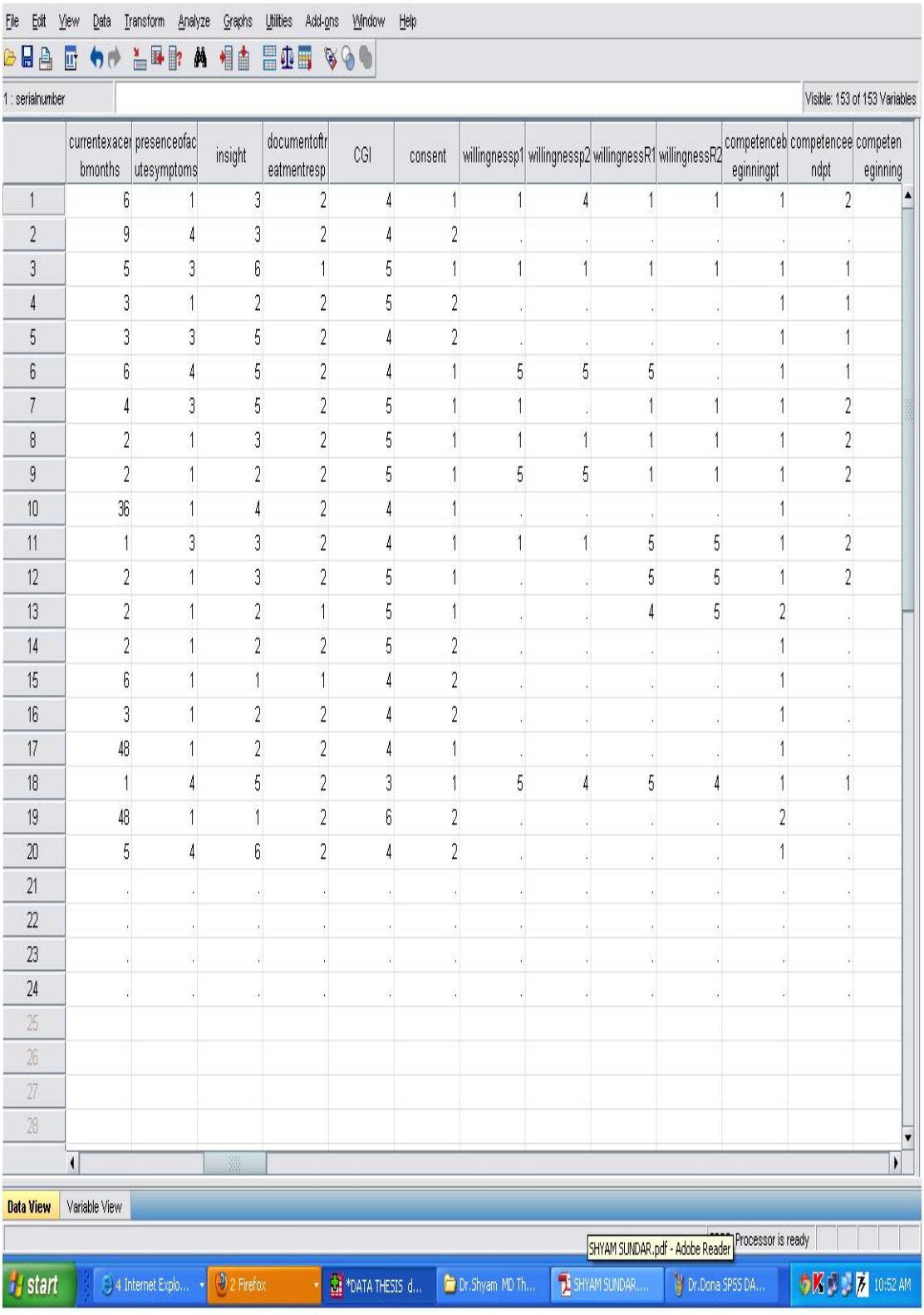

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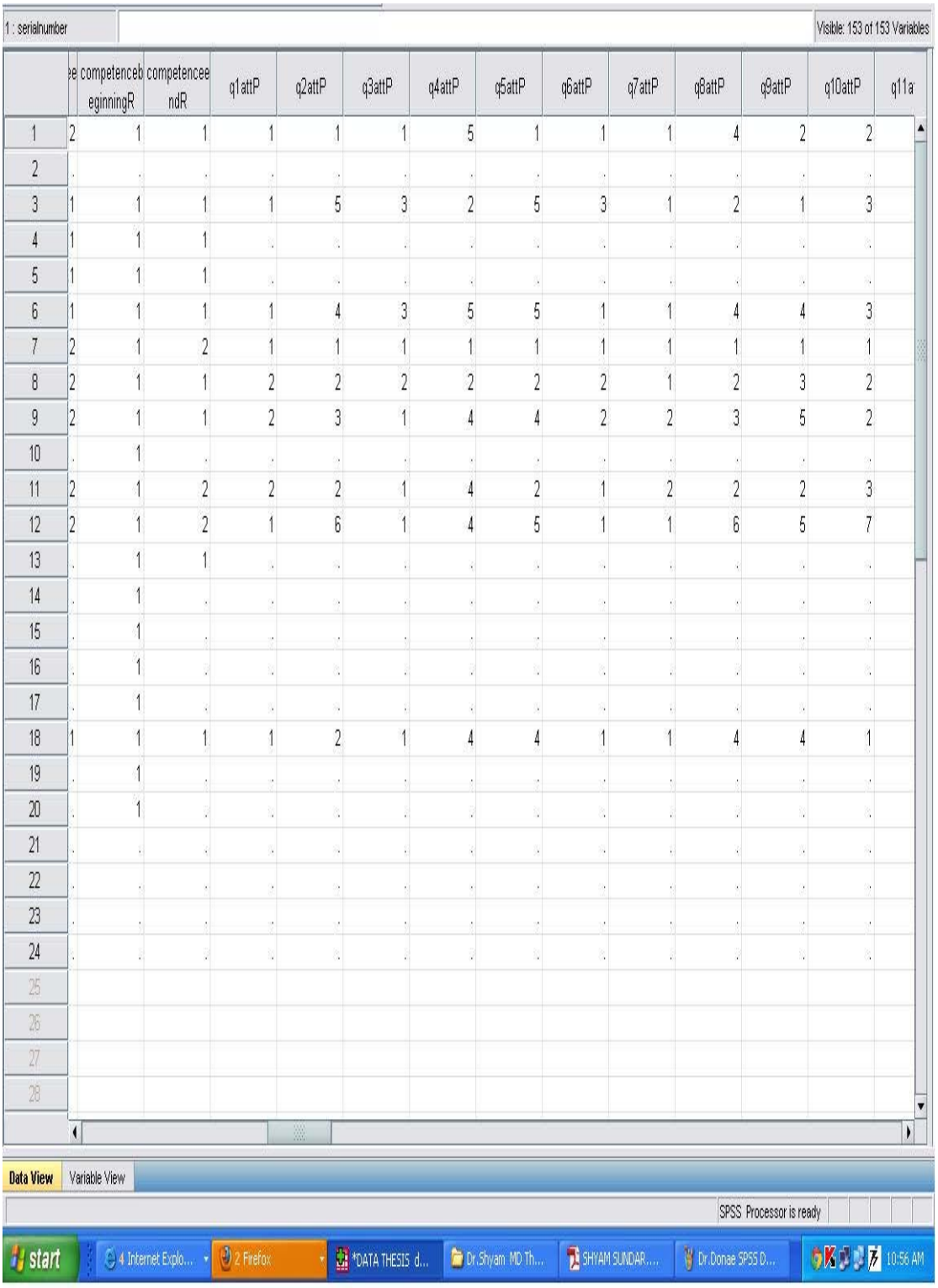
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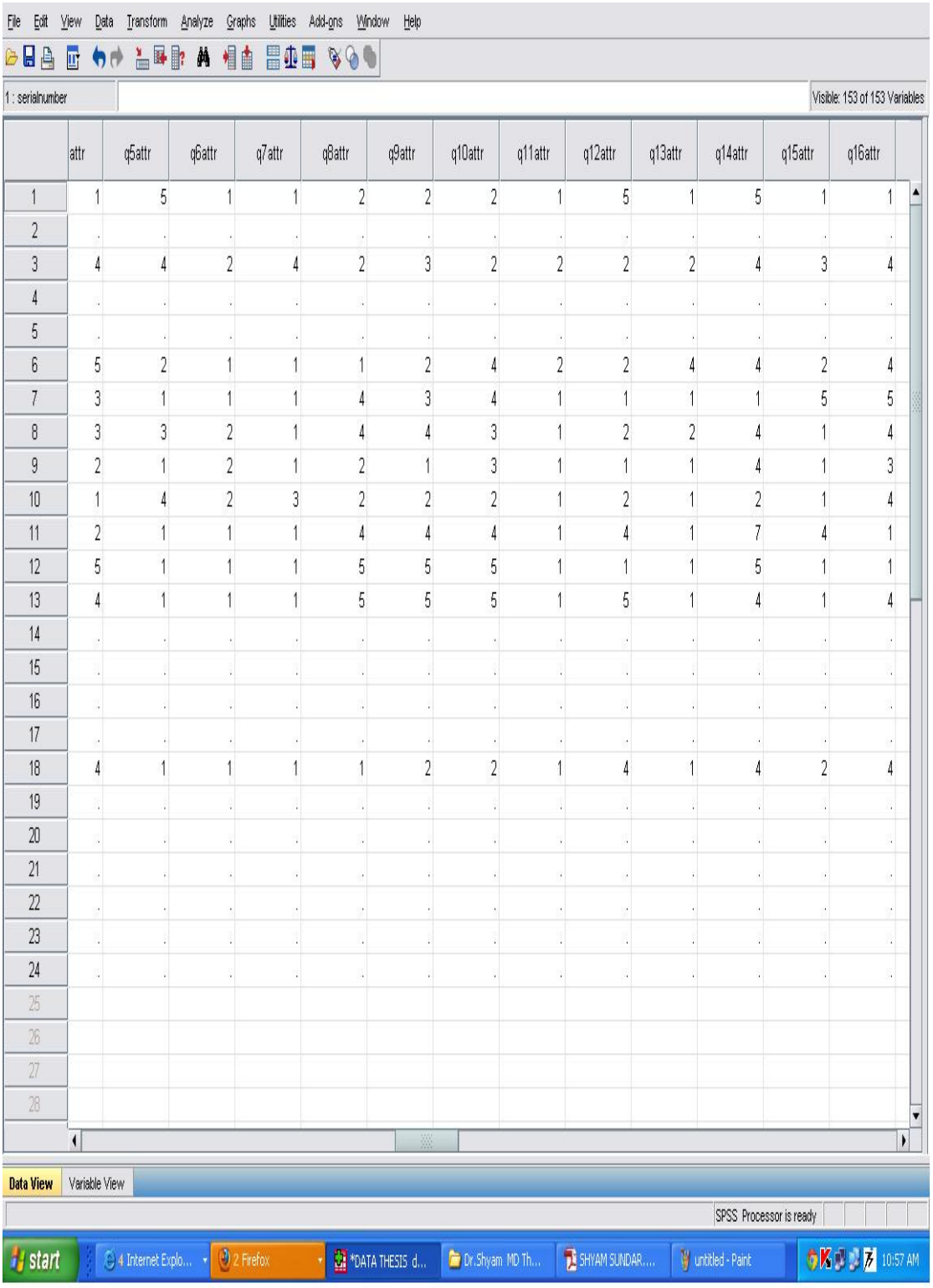

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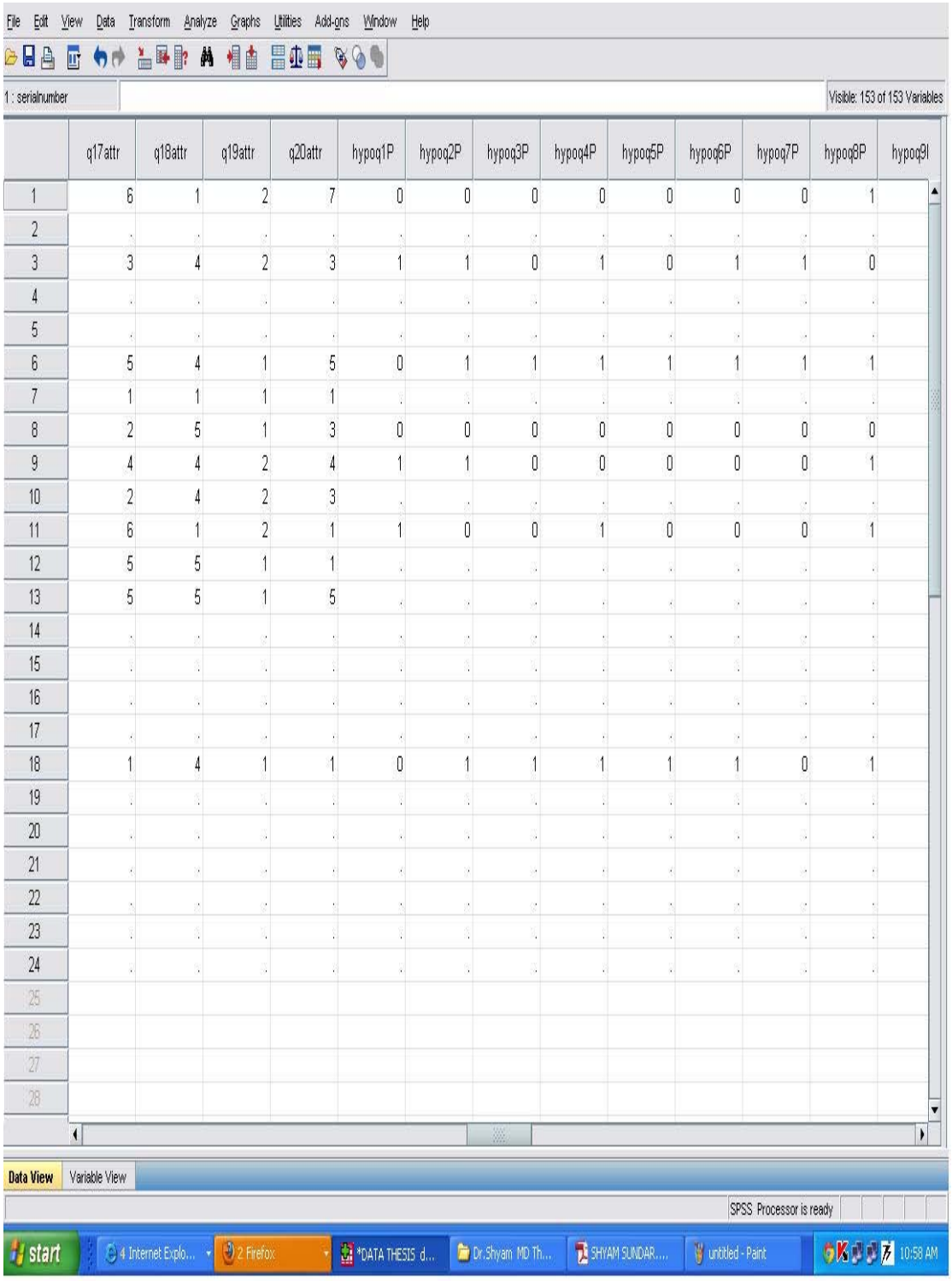

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10	2	4	2	3	.	.	.	.	.	.	.	.	
11	6	1	2	1	1	0	0	1	0	0	0	1	
12	5	5	1	1	.	.	.	.	.	.	.	.	
13	5	5	1	5	.	.	.	.	.	.	.	.	
14	.	.	.	.	.	.	.	.	.	.	.	.	
15	.	.	.	.	.	.	.	.	.	.	.	.	
16	.	.	.	.	.	.	.	.	.	.	.	.	
17	.	.	.	.	.	.	.	.	.	.	.	.	
18	1	4	1	1	0	1	1	1	1	1	0	1	
19	.	.	.	.	.	.	.	.	.	.	.	.	
20	.	.	.	.	.	.	.	.	.	.	.	.	
21	.	.	.	.	.	.	.	.	.	.	.	.	
22	.	.	.	.	.	.	.	.	.	.	.	.	
23	.	.	.	.	.	.	.	.	.	.	.	.	
24	.	.	.	.	.	.	.	.	.	.	.	.	
25													
26													
27													
28													

Appendix – 3c

கற்பனை RCT ஆய்வில் பங்குக் கொள்ளும் மருத்துவர்களுக்கும் மற்ற ஊழியருக்கும் இந்த கேள்விகள் விரிவாக விளக்குதல் முதல் கட்ட விரிவான ஆராய்ச்சி

1. ஏற்கனவே உங்களுக்கு இந்தராய்ச்சியைப் பற்றி எடுத்துரைக்கப்பட்டிக்கின்ற நீங்கள் எவ்வளவு தூரம் இதில் பங்குபெற அல்லது ஒத்துழைப்பு தர விரும்புகிறீர்களா?

பங்கு பெறுவதில் விருப்பமில்லை // விருப்பமில்லை ஆனாலும் பங்கு பெறுதல்// தெரியவில்லை // அரை குறை விருப்பம் // பங்கு பெறுவதில் விருப்பம

2. **திறந்த முடிவில் உங்கள் விருப்பத்திற்கு விடப்பட்ட கேள்விகள்**

- உங்களுடைய சரியான பதில்களுக்கு காரணங்கள் ஏதாவது உள்ளதா

எடுத்தரைத்தல்: இவ்வாய்வில் தரப்படும் இந்த பதில்கள் உங்களுக்கு தேவையாதை கொடுக்கப்படுகின்றதா

குறிப்பிட்டு எடுத்தரைத்தல்: வழக்கமாக கொடுக்கும் மருந்துகள் தொடர வேண்டும் என்று உண்மையில் உங்கள் முடிவை மாற்ற முடிந்ததா கவலையா?

இந்தாய்வில் இரத்த பரிசோதனை மேற்க் கொள்ள வேண்டும் என்ற கவலையாக இருந்ததா?

இந்தாய்வில் ECG பரிசோத்தனை மேற்க் கொள்ள வேண்டும் என்ற கவலையாக இருந்ததா?

இந்தாய்வில் EEG பரிசோதனை மேற்க் கொள்ள வேண்டும் என்ற கவலையாக இருந்ததா?

இந்த கற்பனை ஆய்வைப் பற்றி கவலைபடுவதற்கு வேறு ஏதெனும் காரணங்கள் இருந்ததா?

அதே போல உள்ள மருந்து கொடுப்பது கவலையா உள்ளதா?

இது ஒரு உண்மையான ஆய்வு சோதனையாக இருந்தால் உங்கள் விருப்பத்தை மாற்றியிருப்பீர்களா?

இந்த விரிவாக்க விசாரனை அல்லது முந்தைய சோதனையில் பங்கேற்க விரும்புகிறீர்களா?

நோயாளிகள் மற்றும் உறவினர்கள் இவ்வராய்ச்சி முடிவுகளை வடிவமைக்க உதவிட வேண்டும் என்று நினைக்கிறீர்களா?

Appendix 3d

இந்த RCT-ல் பங்கு பெறுவதால் சில கேள்விகள் கேட்டு வரும் பதில்கள் மூலம் எவ்வளவு தூரம் புரிந்துக் கொண்டீர்கள் என்பதை தெளிவுப்படுத்தும். நிச்சயமற்ற பதில்கள் இருப்பின் பரியும்படியாக விளக்கப்படுவீர்கள்.

சுத்தமாக கேள்விகள் வாசித்து பெறப்படும் பதில்களை பதிவுச் செய்யப்படும். பதிவுச் செய்யப்படும் பதில்கள் மூலம் நீங்கள் எவ்வளவு தூரம் கேற்விகளை உணர்ந்து பதில் அளித்தீர்கள் என்பதை உணர்த்தும்.

1. புதிய மருந்தாகிய GVV278 வழக்கமான மருந்துடன் உட்கொள்ளுவது முந்தின ஆய்வில் பாதுகாப்பானது என்று கணடுபிடிக்கப்பட்டது.

   ஆம் / இல்லை / தெரியவில்லை / மற்றவை

2. இவ்வாய்வில் கலந்துக் கொள்ளும் பட்சத்தில், தற்போது எடுக்கும் மருந்தும் புதிய மருந்தும் சேர்த்து கொடுக்கப்படும்

   ஆம் / இல்லை / தெரியவில்லை / மற்றவை

3. இவ்வாய்வில் கலந்துக் கொள்ளும் பட்சத்தில், புதிய மருந்தாகிய GVV278 உட்கொள்ப்தால் மோசமான நிலையை அடையமாட்டீர்கள்

   ஆம் / இல்லை / தெரியவில்லை / மற்றவை

4. இவ்வாய்வில் கலந்துக் கொள்ளும் பட்சத்தில், வழக்கமான மருந்துக்கு பணம் செலுத்த தேவையில்லை

   ஆம் / இல்லை / தெரியவில்லை / மற்றவை

5. இவ்வாய்வில் கலந்துக் கொள்ளும் பட்சத்தில், மருத்துவமனையில் இருக்கும் போது வாரம் தோறும் EEG மற்றும் ECG எடுக்கப்படும்

   ஆம் / இல்லை / தெரியவில்லை / மற்றவை

   உங்களுடைய நேரத்திற்கும் பதில்களுக்கும் நன்றி. இப்போது உங்களுடைய பதில்களை கலந்தாலோசிப்போம்.

// பக்கம் 30//

இவ்வாய்வில் என்னுடைய முழுஒத்துழைப்பும் கிடைக்க வேண்டும் என்று புரிந்துக் கொண்டேன்.

இந்தாய்வில் பங்கு கொள்வதால் குறைந்தது நான் 4 வாரங்களுக்கு உள்நோயாளியாகவும் ஒவ்வொரு மாத்திரை ஒரு நாள் விதம் மொத்தமாக 8 வாரங்களுக்கு உட்கொள்ள வேண்டும்.

மருத்துவரோ அல்லது எனக்கோ GVV278 அல்லது அதேப் போல உள்ள மருந்து கொடுக்கப்பட நேரிடும். GVV278 அல்லது அதேப் போல உள்ள மருந்து சரிசமமாக கிடைக்கப் வாய்ப்புகள் உள்ளது.

என்னை பற்றியோ நான் கொடுத்த தகவல்களையோ மூன்றாம் நபருக்கோ மருத்துவ பத்திரிக்கையிலோ வெளி வராது மற்றும் பாதுகாக்கப்படும் என்று எடுத்துரைக்கப்பட்டது.

இவ்வாய்விலிருந்து நான் விலகிக் கொண்டாலும் இவ்வாய்விலிருக்கும் ஊழியரோ அல்லது மருத்துவக்குழு உறுப்பினர்களோ என்னுடைய மருத்துவ அறிக்கைப் பட்டியலை பார்ப்பார்கள் அதனால் ஒரு பாதிப்புமில்லை என்று நம்புகிறேன்.

இந்த ஒப்பந்த படிவத்தின் மூலம் என் பங்களிப்பு மற்றும் சூழ்நிலையை புரிந்துக் கொண்டேன்

பெயர்:

கையெப்பம்:

தேதி:

சாட்சியின் பெயர்:

பங்கு பெறுபவரின் உறவு:

தேதி:

முக்கிய உறவின் உடன்பாடு:

_____, ஆகிய நான் _____, கொடுக்கப்பட்ட தகவல்களை வாசித்தும் சந்தேகங்களை தீர்த்துக் கொண்டோம். இதில் பங்கு பெற என் உறவிரை உடன்பட சம்மதிக்கின்றேன்.

இந்த உடன்படிக்கை பாரத்தில் கொடுக்கப்பட்ட சூழ்நிலைக்கும் இவ்வாய்வுக்கும் உடன்பட சம்மதிக்கின்றேன்.

பெயர்:

கையெப்பம்: கையெப்பம்:

தேதி:

பங்கு பெறுபவரின் உறவு:

அறிவிக்கப்பட்ட உடன்பாடு பத்திரம்

ஆய்வின் தலைப்பு: மனநோயாளிகளிடம் உள்ள மன அழுத்தக் குறைபாடு உள்ளவர்களுக்கு GVV278 with placebo மருந்தைக் கொண்டு சூழற்சி முறையீல் பரிசோதனை.

ஆராய்ச்சி செய்பவர்கள் மற்றும் கல்வி நிறுவனம் பற்றிய தகவல்:

டாக்டர் டோனே ஜார்ஜ், டாக்டர் சவ்மில் டோலக்கியா, டாக்டர் பிரதாப் தரியன் . கிறீஸ்துவ மருத்துவக் கல்லூரி வேலூர்.

பெயர்:

கையெப்பம்:

பிறந்த தேதி / வயது (வருடங்களில்):

_____, ஆகிய நான் _____ மகன் / மகள் _____ கொடுக்கப்பட்ட அறிவிப்பு தாளிலிருந்து வாசித்து / வாசித்துக் காண்பிக்கப்பட்டு இது சமபந்தமாக இருந்த சந்தேகங்களை தெளிவிக்கப்பட்டது.

சாதாரணமாக நான் எடுக்கும் மருந்திலிருந்து விலகி ஒரு வாரத்திற்கு மருந்து ஏதும் எடுக்காமல் தேவைப்பட்டால் தூக்க மருந்து கொடுக்கப்படும். நான் எடுக்கும் மருந்து ஒரு வாரத்திற்கு நிறுத்தப்படும் பட்சத்தில் தொந்தரவு இருந்தால் மட்டும் ஆய்வு மருந்தை உட்கொள்ள அழைக்கப்படுக்கிறேன்.

இதில் நான் மனமுவந்து பங்கு கொள்ளுதலும் எப்போழுது வேண்டுமானலும் விலகிக் கொள்வதாலும் இதனால் என்னுடைய சிகிச்சைக்கோ எந்த பாதிப்பும் இல்லாமல் கிடைக்கும் மருத்துவம் தடைபடாது மற்றும் இது என்னுடைய உரிமை என்று புரிந்துக் கொண்டேன்.

4 வாரம் உள் நோயாளியாகவும் ஒரு நாளுக்கு ஒரு மாத்திரை விதம் 8 வாரங்களுக்கு இவ்வாய்வில் கொடுக்கப்படும்.

இரண்டும் ஒன்று போலிருக்கும் பட்சத்தில் நோயாளிகளுக்கோ மருத்துவருக்கோ எனக்கு கொடுக்கும் மருந்து GVV278 அல்லது அதே போல உள்ள மருந்தா என்று தெரியாது. சூழற்சி முறையில் எல்லாருக்கும் சரிசமமாக கொடுக்கப்படும் என்று புரிந்துக் கொண்டேன்.

இவ்வாய்விற்காக வரும் புற நோயாளியாக வரும் பட்சத்தில் இவ்வாய்வு முடிந்து வீட்டிற்கு செல்லும் போது 250 ருபாய் திருப்பி கொடுக்கப்படும். இவ்வாய்விற்காக அதிகம் செலவு செய்திருப்பீர்களானால் ரசீது அல்லது அனுமதி சீட்டு கொடுப்பீர்களானால் அதையும் தர வாய்ப்புள்ளது. இவ்வாய்விற்காக உங்கள் கூட வரும் குடும்ப உறுப்பினருக்கு 250 ருபாய் திருப்பி கொடுக்கப்படும் (ரசீது அல்லது அனுமதி சீட்டு கொடுப்பீர்களானால் அதையும் தர வாய்ப்புள்ளது.) நான்கு வாரம் பிறகு புறநேயாளியாக கருப்படும் நீங்கள் இவ்வாய்விற்காக வந்து போகும் பட்சத்தில் ருபாய் 250 கொடுக்கப்படும்.

இவ்வாய்வு முடிந்தப் பிறது என்ன நிகழும்?

இவ்வாய்வின் முடிவில் நீங்கள் ஆதாயம் பெறலாம் பெறாமலும் போகலாம். கொடுக்கப்பட்ட GVV278 மருந்து உங்களுக்கு உதவிய பட்சத்தில் விருப்பம் இருந்தால் மருத்துவர் இந்த மருந்தை கொடுப்பர். இவ்வாய்விற்கு பிறகு நீங்கள் சிகிச்சை பெறும் மருத்துவர் உங்களுக்கு உசந்த சிகிச்சையே அளிக்கப்படும். ஒரு வேளை நீங்கள் அதே போலிருக்கும் மருந்து உட்கொண்ட பட்சத்தில் GVV278 மருந்து உட்கொண்டவர்கள் பயன் உள்ளதாக இருந்தது என்னும் பட்சத்தில் மருத்துவர் உங்களுக்கு அந்த மருந்தை சிபாரிசு செய்வார். அதற்கு பணம் செலுத்த வேண்டும். இந்தியா முழுவதும் இவ்வாய்வு பணி முடிந்து ஆராய்ந்து பார்த்துப் பிறகு இந்த GVV278 மருந்தை அங்கீகாரம் கொடுக்க ஒரு வருடம் கூட ஆகலாம். அது வரை இந்த மருந்து கையிருப்பு இருக்குமா என்று தெரியாது. மருந்து கம்பெனி மருந்து கையிருப்புக்கு உறுதியளித்துள்ளது.

உங்களுடைய சொந்த விவரங்கள் பாதுகாக்கப்படுமா?

ஆய்வின் முடிவில் மருத்துவ பத்திரிக்கையில் வெளியிடப்படும் உங்கள் பெயர் எங்கும் வெளியிடப்படமாட்டாது. இவ்வாய்வில் பங்குக் கொள்ள ஒப்புக் கொண்டப்பிறகு உங்களுடைய மருத்துவ குறிப்புகளை உங்கள் அனுமதியில்லாமல் பரிசலிக்க உரிமைகள் உண்டு.

கேள்விகள் மற்றும் சந்தேகங்கள் இருப்பின் யாரை தொடர்புக் கொள்வது?

டாக்டர் டோனே ஜார்ஜ், 04162284465, டாக்டர் சவ்மில் டோலக்கியா, டாக்டர் பிரதாப் தரியன் - 0416-2284520 கிறிஸ்துவ மருத்துவக் கல்லூரி மனோத்துவ துறை யூனிட் - 2 அலுவலக நேரத்திலும் அலுவலகத்திலும் தொடர்புக் கொள்ளலாம்.

// பக்கம் - 26 //

எப்போதாவது உங்களுக்கு பிரச்சனை ஏற்படும் போது என்னையோ நர்ஸ் அல்லது மருத்துவரையோ தொடர்பு கொள்ளலாம். உங்களுக்கு சிகிச்சையில் முன்னேற்றம் திருப்தயில்லாத பட்சத்தில் மற்ற மருத்துவரோ அல்லது வழக்கமாக சிகிச்சையளிக்கும் மருத்துவரோ அல்லது நானோ இவ்வாய்விலிருந்து உங்களை விலகி வழக்கமாக எடுக்கும் மருந்துக்கு மாற்றப்படுவீர்கள்.

மாத்திரை உட்கொள்ள தொடங்கி நான்கு வாரம் கழித்து நீங்கள் 50% நன்றாக இருந்தால் வீட்டிற்கு அனுப்பி வைக்கப்படுவீர்கள். வாரத்திற்கு ஒரு முறை என்னாலையோ மற்ற மருத்துவர்களோ உங்களை தோலைப்பேசி மூலம் தொடர்புக் கொண்டு ஏதாவது பக்க விளைவுகளைக் குறித்த அனுபவம் மற்றும் தூக்கம் பசி மனநிலை பலம் மற்றும் அனுதின வேலையைக் குறித்து தோலைப்பேசியின் மூலமாக கேட்கப்பட்டு முன்னேற்றம் உள்ளதா என்று தெரிந்துக் கொள்ளப்படும்.

இந்த ஆய்வின் கடைசி கட்டமாக 8 வாரங்களுக்கு பிறகு நீங்கள் மருத்துமனைக்கு வரவழைக்கப்பட்டு உங்கள் எடை மற்றும் ரத்த பரிசோதனை கண்காணிக்கபட்டு குறித்து வைக்கப்படும்.

நான்கு வாரம் கழித்து 50% வரை குணமாகாத நிலையில் உட்நோயாளியாக கருதப்பட்டு வாரந்தோறும் மதிப்பிடபடுவீர்கள். 50% வரை குணமடைந்த நிலையில் எப்போது வேண்டுமானாலும் வீட்டிற்கு அனுப்பி வைக்கப்பட்டு வாரத்திற்கு ஒரு முறை என்னாலையோ மற்ற மருத்துவர்களோ உங்களை தொடர்புக் கொண்டு ஏதாவது பக்க விளைவுகளைக் குறித்த அனுபவம் மற்றும் தூக்கம் பசி மனநிலை பலம் மற்றும் அனுதின வேலையைக் குறித்து கேட்கப்படும்.

இவ்வாய்வு தொடங்கிய பிறகு விலகிக் கொள்ளலாமா?

இந்தாய்வில் மனமுவந்து பங்கெற்றல் மற்றும் எப்போது வேண்டுமானலும் எந்த காரணம் இருப்பின் விலகிக் கொள்ளலாம். இப்படி செய்வதால் மருத்துவமனையலிருந்து பெறப்படும் உங்கள் சிகிச்சை இதனால் பாதிக்காது. அபாயமான பக்க விளைவுகளோ அல்லது உங்கள் நிலைமை மோசமாகும் பட்சத்தில் மாத்திரை நிறுத்தப்பட்டு கூடுதலாக சிகிச்சை பெறுவீர்கள்.

இவ்வாய்வில் சேதம் வெளிப்படுமாயின் என்னவாகும்?

பெரிய சேதம் வரும் என்று எதிர்ப்பார்க்கவில்லை. அப்படி ஏதெனும் ஏற்ப்பட்டால் சிகிச்சையளிக்கப்படும். ஏதெனும் சேதம் ஏற்பட்டால் சிகிச்சைக்கு பணம் பெற்றுக் கொள்ள மாட்டாது. எங்களால் நஷ்ட ஈடு ஏதுவும் கொடுக்க முடியாது.

இந்த மருந்துக்கு பணம் செலுத்த வேண்டுமா?

8 வாரங்களுக்கு கொடுக்கும் GVV278 மற்றும் அதே போல் இருக்கும் மருந்து இலவசமாகவும் கிடைக்கும். 8 வாரங்களுக்கு உங்கள் மருத்துவ செலவுகள் இலவசமாகவும் வழக்கமாக சிகிச்சைக்கு வரும் நீங்கள் வழக்கமாக சிகிச்சைக்கும் மற்றும் சாப்பாட்டிற்கும் செலவு செய்ய வேண்டும். இவ்வாய்வின் தொடக்கத்தில் பரிந்துரைக்கப்படும் எல்லா மருந்துக்கும் பணம் செலுத்த தேவையில்லை. இவ்வாய்வு தொடர்பாக எடுக்கப்படும் நோயாளியின் விசாரிப்புகள் இலவசமாக வெலுத்தப்படும்.

Appendix 3c

கற்பனை RCT யின் விரிவு: தகவல் மற்றும் ஒப்புதல் படிவம்

கிறிஸ்துவ மருத்துவ கல்லூரி வேலூர்

மனோதத்துவ துறை

இந்த புதிய மருந்தாகிய GVV 278 பற்றி ஏற்கனவே எடுத்துரைக்கப்பட்டது. திரும்பவும் அந்த தகவல்கள் சொல்ல வேண்டுமா? தேளிவாக புரியவில்லை என்றால் திரும்பவும் சொல்லப்படும். புரிந்துக் கொண்ட பட்சத்தில் முதல் கட்ட விரிவான ஆராய்ச்சியாகிய இதில் **உங்கள் பங்கு பற்றி எடுத்துரைக்கப்படும்.**

இவ்வாய்விற்கு ஒப்புதல் அளித்தப்பின் உங்களிடமிருந்து என்ன எதிர்பார்க்கப்படுகிறது?

இவ்வாய்விற்கு ஒப்புதல் அளித்து கையெப்பமிட்டப் பின் உங்களுக்கு வழக்கமாக மருத்துவரிடமிருந்து பெறும் சிகிச்சையும் தோடரும். இவ்வாய்வின் போது 8 வாரங்களுக்கு கொடுக்கப்படும் மருந்துக்கு பணம் செலுத்த தேவையில்லை.

இவ்வாய்வின் தொடக்கமாக காலை உணவிற்கு பிறகு ஒரு நாளுக்கு ஒரு மாத்திரை விதம் 8 வாரங்களுக்கு கொடுக்கப்படும். கொடுக்கப்படும் மாத்திரை GVV அல்லது அதேப் போலிருக்கும் மாத்திரையா என்பது உங்களுக்கோ எங்களுக்கோ தெரியாது. மருத்துவமனனயில் உள் நோயாளியாக இருக்கும் நான்கு வாரம் வரை தினமும் உங்களை பரிசோதித்து பக்க விளைவுகள் இருக்கிற்தா என்று விசாரிக்கப்படுகிறீர்கள்.

இந்த தருணத்தில் உங்கள் நிலையில் மோசமான நிலைக்கு போக வாய்ப்புகள் உண்டு. ஒரு வேளை மோசமாகும் பட்சத்தில் எந்த விதமான அறிகுறிகள் ஏற்படும் என்று தெரியாது. உங்களுடைய நிலையை கண்காணிக்கப்பட்டு உங்களுக்கு சிகிச்சையளிக்கும் மருத்துவரிடமும் விளக்கம் சொல்லப்படும். மோசமான நிலை மற்றும் சௌகரியமில்லாத நிலையிருப்பின் நீங்கள் இவ்வாய்விலிருந்து விலகிக் கொள்ளலாம். எப்போது வேண்டுமானாலும் இதை செய்யலாம் மற்றும் நீங்கள் வழக்கமாக எடுக்கும் மருந்துக்கு மாற்றப்படுவீர்கள். தினமும் உங்கள் தூக்கம் அனுதின வேலை எப்படியுள்ளீர்கள் அதோடு பக்க விளைவுகள் உள்ளதா என்றும் விசாரிக்கப்படுகிறீர்கள். மருத்துவமனையில் உள்ள வரை தினமும் உங்கள் எடை மற்றும் ரத்த அழுத்தம் பரிசோதனை செய்து குறிப்பு எடுக்கப்படும்.

வழக்கமாக எடுக்கும் மருந்துடன் இந்த புதிய மருந்து GVV 278 சேர்த்து கொடுக்கப்படும் மருந்தால் எந்த பிரச்சனையும் ஏற்படக் கூடாது என்பதில் கவனமாக இருப்போம். இதற்க்காக நீங்கள் ஒப்புதல் அளிப்பின் இரத்த பரிசோதனை மூலமாக கல்லீரல் மற்றும் நுரையிரல் எவ்வாறு உள்ளது என்று இவ்வாய்வின் ஆரம்பத்திலும் உள்நோயாளியாக இருக்கும் போது வாரம் ஒரு முறை என்று நான்கு வாரத்திற்க்குத் பிறகு 8 வார முடிவிலும் இவ்வாய்வின் முடிவிலும் எடுக்கப்படும். பரிசோதனை முடிந்தப் பிறகு மீதியுள்ள இரத்தம் தள்ளுபடி செய்யப்படும். அதோடு கூட EEG மூலமாக மூளையின் பயன்பாடு மற்றும் ECGயின் மூலமாக இதய துடிப்பும் இந்த ஆய்வின் தொடக்கத்திலும் முடிவிலும் எடுக்கப்படும். ECG மற்றும் EEG பரிசோதனை சி.எம்.சி மருத்துவமனையிலுள்ள ஆய்வுக் கூடத்தில் சிறப்பு அப்பாயிண்ட்மென்ட் வாங்கி வலிகள் இல்லாமல் எடுக்கப்படும். இந்தாய்வில் பங்குக் கொள்ளும் பட்சத்தில் இதைப் பற்றி மேலும் விரிவாக உங்களுக்கு எடுத்துரைக்கப்படும்.

2. **திறந்த முடிவில் உங்கள் விருப்பத்திற்கு விடப்பட்ட கேள்விகள்**

உங்களுடைய சரியான பதில்களுக்கு காரணங்கள் ஏதாவது உள்ளதா

எடுத்தரைத்தல்: இவ்வாய்வில் தரப்படும் இந்த பதில்கள் உங்களுக்கு தேவையாதை கொடுக்கப்படுகின்றதா

குறிப்பிட்டு எடுத்தரைத்தல்: வழக்கமாக கொடுக்கும் மருந்துகள் நிறுத்தப்படும் என்ற கவலையா உள்ளதா?

இந்தாய்வில் பங்கு பெறுவதால் மருந்துகளை தெர்ந்தெடுக்க முடியாது என்ற கவலையா?

உங்கள் மருத்துவருக்கும் மருந்தை தெர்ந்தெடுக்க முடியாது என்ற கவலையா?

அதே போல உள்ள மருந்து கொடுப்பது கவலையா உள்ளதா?

கற்பனையில் பங்கு கொண்ட நீங்கள் உண்மையாள ஆராய்ச்சியில் பங்கு பெறுவீர்கள்

இந்த மாதிரி ஆராய்ச்சி நடக்க வேண்டும் என்று விரும்புகிறீர்களா?

வழக்கமாக உங்களை பரிசோதிக்கும் மருத்துவர் பரிந்துரைத்தால் சரி என்று ஒப்புக்கொண்டீர்களா?

6. நீங்கள் இந்த ஆய்வில் பங்கு பெறும் பட்சத்தில் கொடுக்கப்படும் மருந்து எதுவாக மேலானமாக உணர்ந்தீர்களா?

   சரி / தவறு /தெரியவில்லை/ மற்றவை

7. பங்குக் கொள்ளும் பட்சத்தில் நீங்கள் GVV278 மருந்தை உட்கொள்வதால் எப்படியிருந்தாலும் மோசமான நிலைமைக்கு வரமாட்டீர்கள்

   சரி / தவறு /தெரியவில்லை / மற்றவை

8. பங்குக் கொள்ளும் பட்சத்தில் உங்களுக்கு இலவச உணவும் ஒரு நாளுக்கு 200 ருபாய் கொடுக்கப்படும்

   சரி / தவறு /தெரியவில்லைல/ மற்றவை

9. பங்குக் கொள்ளும் பட்சத்தில் உங்களுக்கு உட்நோயாளியாக இருக்கும் போது வாரம்தோறும் ரத்தப் பரிசோதனன செய்யப்படும்.

   சரி / தவறு /தெரியவில்லை/ மற்றவை

10. பங்குக் கொள்ளும் பட்சத்தில் உங்களுக்கு புதிய மருந்தைப் போல இருக்கும் மருந்தை உட்கொள்வதால் நிலைமை மோசமாக உள்ளதா

    சரி / தவறு /தெரியவில்லை/ மற்றவை

கேள்விகளுக்கு உங்கள் பதில்களையும் நேரத்தையும் கொடுத்ததுற்க்கு நன்றி. இப்போது அதை கொண்டு உங்களுடன் உரையாட் போகின்றேன்

Appendix – 3a

கற்பனை RCT ஆய்வில் பங்குக் கொள்ளும் மருத்துவர்களுக்கும் மற்ற ஊழியருக்கும் இந்த கேள்விகள் விரிவாக விளக்குதல்

1. ஏற்கனவே உங்களுக்கு இந்தராய்ச்சியைப் பற்றி எடுத்துரைக்கப்பட்டீர்கின்ற நீங்கள் எவ்வளவு தூரம் இதில் பங்குபெற அல்லது ஒத்துழைப்பு தர விரும்புகிறீர்களா?

   பங்கு பெறுவதில் விருப்பமில்லை // விருப்பமில்லை ஆனாலும் பங்கு பெறுதல்// தெரியவில்லை // அரை குறை விருப்பம் // பங்கு பெறுவதில் விருப்பம

Appendix 3a

Comprehension of information for the Hypothetical RCT on GVV278

RCT யில் பங்குக் கொள்ளும் உங்களிடத்தில் சில கேள்விகள் கேட்கப்பட்டு எவ்வளவு தூரம் புரிந்து வைத்துள்ளீர்கள் என்பதை புரிந்துக் கொள்ளவும் அழைக்கப்படுகிறீர்கள். கேட்கப்படும் கேள்விகள் புரியவில்லை என்றால் உங்களுக்கு புரியும்படி விளக்கப்படும்.

சத்தமாக கேள்விகள் வாசித்து பெறப்படும் பதில்கள் குறிப்பெடுத்தும் ரெக்காடரிலும் பதிவுச் செய்யப்படும். இதன் மூலம் பதில்களை சரியாக புரிந்துக் கொள்வதற்காக.

1. மன அழுத்தத்தில் இருக்கும் மனநோயாளிக்கு இப்போது வழங்கப்படும் மருந்தைக் காட்டிலும் இந்த மருந்து மிகவும் நன்றாகயுள்ளது என்று முந்தைய ஆராய்ச்சியில் இதற்கு புதிய மருந்து GVV278 கண்டுபிடிக்கப்பட்டது

   சரி / தவறு /தெரியவில்லை/ மற்றவை

2. பங்குக் கொள்ளும் பட்சத்தில் நானோ அல்லது உங்களுக்கு சிகிச்சையளிக்கும் மருத்துவரோ GVV278 அல்லது அதேப் போல இருக்கும் மருந்தோ உங்களுக்கு கொடுக்க தீர்மானிப்போம்.

   சரி / தவறு /தெரியவில்லை / மற்றவை

3. பங்குக் கொள்ளும் பட்சத்தில் வழக்கமாக எடுக்கும் மருந்தும் இந்த புதிய மருந்தும் கொடுக்கப்படுவீர்கள்

   சரி / தவறு /தெரியவில்லை / மற்றவை

4. பங்குக் கொள்ளும் பட்சத்தில் உங்களுக்கு கொடுக்கப்படும் மருந்து என்ன மருந்து என்பதை மருத்துவரையோ நர்சையோ மருந்து கொடுப்பவரையோ கேட்டு தெரிந்துக் கொள்ளலாம்

   சரி / தவறு /தெரியவில்லை / மற்றவை

5. பங்குக் கொள்ளும் பட்சத்தில் நீங்கள் 4 வாரங்களுக்கு இந்த மருந்தை உட்கொள்ளப்படுவீர்கள்

   சரி / தவறு /தெரியவில்லை / மற்றவை

இந்த ஆய்வினால் எந்த ஆதாயமோ சேதமோ ஏற்பட்டல் இழப்பீடு இல்லை மற்றும் சிகிச்சைக்கு பணம் செலுத்த வேண்டாம் என்பதை புரிந்துக் கொண்டேன்.

8 வாரங்களுக்கு கொடுக்கும் GVV278 மற்றும் அதே போல் இருக்கும் மருந்து இலவசமாகவும் கிடைக்கும். GVV278 மருந்து உட்கொண்டவர்கள் பயன் உள்ளதாக இருந்தது என்னும் பட்சத்தில் மருத்துவர் உங்களுக்கு அந்த மருந்தை சிபாரிசு செய்வார். அதற்கு பணம் செலுத்த வேண்டும் இந்த மருந்து கையிருப்பு இருக்குமா என்று தெரியாது என்பதையும் புரிந்துக் கொண்டேன்.

ஆய்வின் முடிவில் மருத்துவ பத்திரிக்கையில் வெளியிடப்படும் போது பெயர் எங்கும் வெளியிடப்படமாட்டாது. பாதுகாப்பாக இருக்கும் என்று நம்புகிறேன்.

நான் பாதியில் விலகினாலும் இவ்வாய்க்குழு எப்போழுது வேண்டுமானாலும் என்னுடைய மருத்துவ பதிவை பார்க்க என்னுடைய அனுமதியோ / என்னுடைய உறவினர் அனுமதியோ தேவைப்படாது என்பதை புரிந்துக் கொண்டேன்.

இவ்வாய்வில் பங்கு பெறவும் தகவல் படிவத்தில் உள்ள விதிகளையும் உடன்படுகிறேன்.

பெயர்:

கையெப்பம்:

தேதி:

சாட்சியின் பெயர்:

பங்குபெறுபவரின் உறவுமுறை:

தேதி:

முக்கிய உறவின் உடன்பாடு:

<u>உறவினரின் ஒப்புதல்</u>

_____, ஆகிய நான் _____
உறவினருக்கு வாசித்து காண்பிக்கப்பட்டு சந்தேகங்கள் தீர்க்கப்பட்டு இதில் பங்குக் கொள்ள உடன்படுகிறேன்.

இந்த ஆய்வில் என்னுடைய பங்கு பெறுதல் மற்றும் இந்த தகவல் படிவத்தில் உள்ள விதிகள் எடுத்துரைக்கப்பட்டது.

பெயர்:

கையெப்பம்:

தேதி:

பங்குபெறுபவரின் உறவுமுறை:

அறிவக்கப்பட்ட உடன்பாடு பத்திரம்

ஆய்வின் தலைப்பு: மனநோயாளிகளிடம் உள்ள மன அழுத்தக் குறைபாடு உள்ளவர்களுக்கு GVV278 with placebo மருந்தைக் கொண்டு சூழற்சி முறையில் பரிசோதனை.

ஆராய்ச்சி செய்பவர்கள் மற்றும் கல்வி நிறுவனம் பற்றிய தகவல்:

டாக்டர் டோனே ஜார்ஜ், டாக்டர் சவ்மில் டோலக்கியா, டாக்டர் பிரதாப் தரியன் கிறிஸ்துவ மருத்துவக் கல்லூரி வேலூர்.

பெயர்:

கையெப்பம்:

பிறந்த தேதி / வயது (வருடங்களில்):

_____, ஆகிய நான் _____ மகன் / மகள் _____ கொடுக்கப்பட்ட அறிவிப்பு தாளிலிருந்து வாசித்து / வாசித்துக் காண்பிக்கப்பட்டு இது சமபந்தமாக இருந்த சந்தேகங்களை தெளிவிக்கப்பட்டது.

சாதாரணமாக நான் எடுக்கும் மருந்திலிருந்து விலகி ஒரு வாரத்திற்கு மருந்து ,ஏதும் எடுக்காமல் தேவைப்பட்டால் தூக்க மருந்து கொடுக்கப்படும். நான் எடுக்கும் மருந்து ஒரு வாரத்திற்கு நிறுத்தப்படும் பட்சத்தில் தொந்தரவு இருந்தால் மட்டும் ஆய்வு மருந்தை உட்கொள்ள அழைக்கப்படுக்கிறேன்.

இதில் நான் மனமுவந்து பங்கு கொள்ளுதலும் எப்போழுது வேண்டுமானலும் விலகிக் கொள்வதாலும் இதனால் என்னுடைய சிகிச்சைக்கோ எந்த பாதிப்பும் இல்லாமல் கிடைக்கும் மருத்துவம் தடைபடாது மற்றும் இது என்னுடைய உரிமை என்று புரிந்துக் கொண்டேன்.

4 வாரம் உள் நோயாளியாகவும் ஒரு நாளுக்கு ஒரு மாத்திரை விதம் 8 வாரங்களுக்கு இவ்வாய்வில் கொடுக்கப்படும்.

இரண்டும் ஒன்று போலிருக்கும் பட்சத்தில் நோயாளிகளுக்கோ மருத்துவருக்கோ எனக்கு கொடுக்கும் மருந்து GVV278 அல்லது அதே போல உள்ள மருந்தா என்று தெரியாது. சூழற்சி முறையில் எல்லாருக்கும் சரிசமமாக கொடுக்கப்படும் என்று புரிந்துக் கொண்டேன்.

இவ்வாய்வில் என்னுடைய முழுஒத்துழைப்பும் கிடைக்க வேண்டும் என்று புரிந்துக் கொண்டேன்.

கேள்விகள் மற்றும் சந்தேகங்கள் இருப்பின் யாரை தொடர்புக் கொள்வது?

டாக்டர் டோனே ஜார்ஜ் 0416 228 4485 , டாக்டர் சவ்மில் டோலக்கியா, டாக்டர் பிரதாப் தரியன் - 0416-2284520 கிறிஸ்துவ மருத்துவக் கல்லூரி மனோத்துவ துறை யூனிட் - 2 அலுவலக நேரத்திலும் அலுவலகத்திலும் தொடர்புக் கொள்ளலாம்.

இவ்வாய்வு தொடங்கிய பிறகு விலகிக் கொள்ளலாமா?

இந்தாய்வில் மனமுவந்து பங்கெற்றல் மற்றும் எப்போது வேண்டுமானலும் எந்த காரணம் இருப்பின் விலகிக் கொள்ளலாம். இப்படி செய்வதால் மருத்துவமனையலிருந்து பெறப்படும் உங்கள் சிகிச்சை இதனால் பாதிக்காது. அபாயமான பக்க விளைவுகளோ அல்லது உங்கள் நிலைமை மோசமாகும் பட்சத்தில் மாத்திரை நிறுத்தப்பட்டு கூடுதலாக சிகிச்சை பெறுவீர்கள்.

இவ்வாய்வில் சேதம் வெளிப்படுமாயின் என்னவாகும்?

பெரிய சேதம் வரும் என்று எதிர்ப்பார்க்கவில்லை. அப்படி ஏதெனும் ஏற்ப்பட்டால் சிகிச்சையளிக்கப்படும். ஏதெனும் சேதம் ஏற்பட்டால் சிகிச்சைக்கு பணம் பெற்றுக் கொள்ள மாட்டாது. எங்களால் நஷ்ட ஈடு ஏதுவும் கொடுக்க முடியாது.

இந்த மருந்துக்கு பணம் செலுத்த வேண்டுமா?

8 வாரங்களுக்கு கொடுக்கும் GVV278 மற்றும் அதே போல் இருக்கும் மருந்து இலவசமாகவும் கிடைக்கும். 8 வாரங்களுக்கு உங்கள் மருத்துவ செலவுகள் இலவசமாகவும் வழக்கமாக சிகிச்சைக்கு வரும் நீங்கள் சாப்பாட்டிற்கு செலவு செய்ய வேண்டும். இவ்வாய்விற்காக வரும் புற நோயாளியாக வரும் பட்சத்தில் இவ்வாய்வு முடிந்து வீட்டிற்கு செல்லும் போது 250 ருபாய் திருப்பி கொடுக்கப்படும். இவ்வாய்விற்காக அதிகம் செலவு செய்திருப்பீர்களானால் ரசீது அல்லது அனுமதி சீட்டு கொடுப்பீர்களானால் அதையும் தர வாய்ப்புள்ளது. இவ்வாய்விற்காக உங்கள் கூட வரும் குடும்ப உறுப்பினருக்கு 250 ருபாய் திருப்பி கொடுக்கப்படும் (ரசீது அல்லது அனுமதி சீட்டு கொடுப்பீர்களானால் அதையும் தர வாய்ப்புள்ளது.) நான்கு வாரம் பிறகு புறநேயாளியாக கருப்படும் நீங்கள் இவ்வாய்விற்காக வந்து போகும் பட்சத்தில் ருபாய் 250 கொடுக்கப்படும்.

இவ்வாய்வு முடிந்தப் பிறது என்ன நிகழும்?

இவ்வாய்வின் முடிவில் நீங்கள் ஆதாயம் பெறலாம் பெறாமலும் போகலாம். கொடுக்கப்பட்ட GVV278 மருந்து உங்களுக்கு உதவிய பட்சத்தில் விருப்பம் இருந்தால் மருத்துவர் இந்த மருந்தை கொடுப்பர். இவ்வாய்விற்கு பிறகு நீங்கள் சிகிச்சை பெறும் மருத்துவர் உங்களுக்கு உசந்த சிகிச்சையே அளிக்கப்படும். ஒரு வேளை நீங்கள் அதே போலிருக்கும் மருந்து உட்கொண்ட பட்சத்தில் GVV278 மருந்து உட்கொண்டவர்கள் பயன் உள்ளதாக இருந்தது என்னும் பட்சத்தில் மருத்துவர் உங்களுக்கு அந்த மருந்தை சிபாரிசு செய்வார். அதற்கு பணம் செலுத்த வேண்டும். இந்தியா முழுவதும் இவ்வாய்வு பணி முடிந்து ஆராய்ந்து பார்த்துப் பிறகு இந்த GVV278 மருந்தை அங்கீகாரம் கொடுக்க ஒரு வருடம் கூட ஆகலாம். அது வரை இந்த மருந்து கையிருப்பு இருக்குமா என்று தெரியாது. மருந்து கம்பெனி மருந்து கையிருப்புக்கு உறுதியளித்துள்ளது.

உங்களுடைய சொந்த விவரங்கள் பாதுகாக்கப்படுமா?

ஆய்வின் முடிவில் மருத்துவ பத்திரிக்கையில் வெளியிடப்படும் உங்கள் பெயர் எங்கும் வெளியிடப்படமாட்டாது. இவ்வாய்வில் பங்குக் கொள்ள ஒப்புக் கொண்டப்பிறகு உங்களுடைய மருத்துவ குறிப்புகளை உங்கள் அனுமதியில்லாமல் பரிசீலிக்க உரிமைகள் உண்டு.

இவ்வாய்விற்கு ஒப்புதல் அளித்தப்பின் உங்களிமிருந்து என்ன எதிர்பார்க்கப்படுகிறது?

இவ்வாய்விற்கு ஒப்புதல் அளித்து கையெப்பமிட்டப் பின் உங்களுக்கு வழக்கமாக பெறும் சிகிச்சையிலிருந்து மாற்றப்பட்டு தூக்கமின்மை இருக்குமானால் ஒரு வாரத்திற்கு மிதமாக ஆற்றுகின்ற மருந்து வழங்கப்படும். உங்கள் உடம்பில் இதற்கு முன்பு சாப்பிட்ட மருந்துகள் இருக்காது என்று உறுதி செய்யப்படுகிறது. ஒரு வாரம் கழித்து உங்களை பரிசோதனை செய்யும் போது போதுமான அறிகுறிகள் இல்லாத பட்சத்தில் உங்கள் பங்கு இத்துடன் முடிவடைந்து உங்களுக்கு சிகிச்சையளிக்கும் குழுவுடன் கலந்து ஆலோசித்து வாடிக்கையான மருத்துகள் தொடரலாம்.

ஒரு வாரம் கழித்து அறிகுறிகள் தொடருமாயின் ஒரு நாளுக்கு ஒரு மாத்திரை விதம் காலை உணவிற்குப் பிறகு 8 வாரங்களுக்கு கொடுக்கப்படும். கொடுக்கப்படும் மாத்திரை GVV அல்லது அதேப் போலிருக்கும் மாத்திரையா என்பது உங்களுக்கோ எங்களுக்கோ தெரியாது. மருத்துவமனையில் உள் நோயாளியாக இருக்கும் வரையில் நான்கு வாரம் வரை தினமும் உங்களை பரிசோதித்து பக்க விளைவுகள் இருக்கிறதா என்று விசாரிக்கப்படுகிறீர்கள்.

இந்த தருணத்தில் அதிக கோபம், தூக்கமின்மை, அமைதியின்மை போன்ற காரியங்கள் அனுபவிக்க வாய்ப்புள்ளது. உங்களை நன்றாக கண்கணித்து உங்களுக்கு வழக்கமான சிகிச்சையளிக்கும் மருத்துவரிடமும் உங்கள் நிலை அறிவிக்கப்படும். அசௌகரியமோ மோசமான நிலை ஏழும் பட்சத்தில் இவ்வாய்பிலிருந்து விலகிக் கொள்ளலாம். இவ்வாய்விலிருந்து எப்போது வேண்டுமானாலும் வழக்கமாக பெறும் மருந்துக்கு மாற்றப்படுவீர்கள். தினமும் உங்கள் தூக்கம் அனுதின வேலை எப்படியுள்ளீர்கள் அதோடு பக்க விளைவுகள் உள்ளதா என்றும் விசாரிக்கப்படுகிறீர்கள் மருத்துவமனையில் உள்ள வரை தினமும் உங்கள் எடை மற்றும் ரத்த அழுத்தம் பரிசோதனை செய்து குறிப்பு எடுக்கப்படும். இவ்வாய்விற்கு ரத்த பரிசோதனையோ கூடுதலாக வேறு எந்த பரிசோதனையோ செய்ய வேண்டியதில்லை.

எப்போதாவது உங்களுக்கு பிரச்சனை ஏற்படும் போது என்னையோ நர்ஸ் அல்லது மருத்துவரையோ தொடர்பு கொள்ளலாம். உங்களுக்கு சிகிச்சையளிக்கும் முறை திருப்தியாக இல்லாத பட்சத்தில் நானோ மற்ற மருத்துவரோ இவ்வாய்விலிருந்து விலகி வழக்கமாக பெறும் மருந்துக்கு மாற்றப்படுவீர்கள்.

மாத்திரை உட்கொள்ள தொடங்கி நான்கு வாரம் கழித்து நீங்கள் 50% நன்றாக இருந்தால் வீட்டிற்கு அனுப்பி வைக்கப்படுவீர்கள். வாரத்திற்கு ஒரு முறை என்னாலையோ மற்ற மருத்துவர்களோ உங்களை தொடர்புக் கொண்டு ஏதாவது பக்க விளைவுகளைக் குறித்த அனுபவம் மற்றும் தூக்கம், பசி, மனநிலை, பலம் மற்றும் அனுதின வேலையைக் குறித்து தோலைப்பேசியின் மூலமாக கேட்கப்படும்.

இந்த ஆய்வின் கடைசி கட்டமாக 8 வாரங்களுக்கு பிறகு நீங்கள் மருத்துமனைக்கு வரவழைக்கப்பட்டு உங்கள் எடை மற்றும் ரத்த பரிசோதனை கண்காணிக்கபட்டு குறித்து வைக்கப்படும்.

நான்கு வாரம் கழித்து 50% வரை குணமாகாத நிலையில் உட்நோயாளியாக கருதப்பட்டு வாரந்தோறும் மதிப்பிடபடுவீர்கள். 50% வரை குணமடைந்த நிலையில் எப்போது வேண்டுமானாலும் வீட்டிற்கு அனுப்பி வைக்கப்பட்டு வாரத்திற்கு ஒரு முறை என்னாலையோ மற்ற மருத்துவர்களோ உங்களை தொடர்புக் கொண்டு ஏதாவது பக்க விளைவுகளைக் குறித்த அனுபவம் மற்றும் தூக்கம், பசி மனநிலை பலம் மற்றும் அனுதின வேலையைக் குறித்து கேட்கப்படும்.

இந்த GVV278 மருந்துகள் பின் விளைவுகளை ஏற்படுத்துமா?

இந்த GVV278 மருந்துகள் உட்கொண்ட ஒரு சிலருக்கு தலைவலி பரபரப்பான நிலைமை வாந்தி வயிற்றுப் போக்கு மற்றும் வயிற்று வலி போன்றவை ஏற்பட்டது. ஆனால் அது மிதமானதாகவும் தற்காலிகமானதாகவும் இருந்தது. திடீரென்று இந்த GVV278 மருந்துகள் உட்கொள்வதை நிறுத்தும் பட்சத்தில் எந்த பிரச்சனைகளும் ஏற்படாது. ஒரு வேளை ரத்த அழுத்தம் மிதமாக ஏறும் ஆனால் ஆபத்தில்லாதது. இருதயத்திற்கு எந்த பாதிப்பும் ஏற்படுத்தாது.

இந்த GVV278 விளைவு திட்டப்படுத்துவதற்க்கு இந்தராய்ச்சி எப்படி உதவுகிறது?

இந்த சீரற்ற கட்டுபாடு சோதனை முற்றிலும் வடிவமைக்கப்பட்டது. இங்கு ஆய்விற்கு தகுதியான ஒவ்வொரு நோயாளியிடம் ஒப்புதல் பெறப்படும். இந்த ஆய்வில் பங்கு பெறும் இவர்களுக்கு அடையாளம் வழங்கப்படும். இவர்களுக்கு 8 வாரத்திற்கு தினமும் காலை உணவு கொடுத்தப் பிறகு மாத்திரை வழங்கப்படும். அதில் மீதி உள்ள பாதி மாத்திரைகள் அடையாள குறியிடப்பட்டு ஆனால் GVV 278 கலக்கப்படாதது. அதில் சிறிய அளவு சுக்ரோஸ் (சர்க்கரை) ஆனால் இதை எடுத்துக் கொள்வதால் எந்த பக்க விளைவும் இல்லை. இம்முறை தேர்வில் யார் GVV 278 அல்லது போலி மாத்திரை உட்கொண்டவர்களை கண்டறிய கணினியில் மருந்தாளுனர் மூலம் குறியிடு வழங்கப்படும். இதை சுவிட்சர்லாந்தில் உள்ள ஒரு மருத்துவ நிறுவனத்தின் மூலம் வழங்கக்கட்டது. பிறகு அவர்கள் தொடர் எண்களைக் கொண்ட அட்டைப் பெட்டிகளை (மருந்துகள் அடங்கியது) GVV (அல்லது) போலி மருந்தை ஒரு வாரத்திற்கு தொடர் எண் குறியிடு மூலம் தயார் செய்து அனுப்பி வைக்கப்படும்.

இந்த ஆய்வில் பங்கு பெறும் மருத்துவமனை மருத்துவர்களுக்கு இந்த குறியிட்டு எண் பற்றியோ (அல்லது) மாத்திரை என்ன என்பது பற்றியோ தெரியாது. இவை அனைத்தும் (தகவல்கள்) சோதனையில் ஈடுபட்டிருக்கும் மருந்தை வழங்கும் மருத்துவ நிறுவனத்திற்கு மட்டுமே தெரியும்.

மருந்துவமனை மருத்துவர்களுக்கு தொடர் எண்கள் குறியிடு செய்யப்பட்ட மருந்து பெட்டிகள் மூலம் மருந்துகள் வழங்கப்படுகின்றது. இந்த ஆய்வை 8 வாரங்களுக்கு நோயாளிக்கு கொடுக்கப்பட்டு அந்தந்த மருத்துவமனை மருத்துவர்களையே பணியமர்த்திட வேண்டும்.

நாம் இம்முறை மூலம் எதிர்பார்த்து அனைத்து மக்களிடமும் அறிகுறிகளின் தீவிரத்தையும் அதாவது குறைவான அறிகுறி உள்ளவர்களுக்கும் அல்லது அதிகமான அறிகுறி உள்ளவர்களுக்கும் GVV278 அல்லது போலி மாத்திரையை பெற சமமான வாய்ப்பு கிடைக்கும் என்று எதிர்ப்பார்க்கின்றோம்.

இரண்டும் ஒன்று போலிருக்கும் பட்சத்தில் நோயாளிகள் மருத:துவரிடம் மருந்து உட்கொள்வதால் ஆதாயமா அல்லது பக்க விளைவுகள் என்று மருத்துவரிடம் கூறும் பட்சத்தில் மருத்துவருக்கே தெரியாமல் யாருக்கு GVV278 மாத்திரை அல்லது மாதிரியுள்ள மருந்து கொடுக்கப்பட்டது என்று மருத்துவமனையிலிருப்போருக்கும் யாருக்கும் தெரியாது. முதல் மாதத்தின் ஒவ்வொரு வாரமும் மற்றும் 8ம் வார முடிவிலும் அறிகுறிகளையும் பக்க விளைவுகளையும் வைத்து கணிக்கப்படும். இதன் மூலம் குறிகள் மீது மதிப்பை எழுதி எது சிறந்த மருந்து என்றும் எது பக்க விளைகள் அதிகம் என்று கணிக்கப்படும்.

இந்த முறை மூலம் மனஅழுத்தம் உள்ள மனநோயாளிகளுக்கு GVV யால் விளைவுகளை பற்றி அறிந்துக் கொள்ள முடியும்.

Appendix- 3

கிறிஸ்துவ மருத்துவ கல்லூரி வேலூர்

மனோதத்துவ துறை

மக்களின் மனஅழுத்தம் தொடர்பான உளவியல் நோய்களின் அறிகுறிகளை குறைக்க GVV 278 உடன் போலி மருந்துடன் ஒப்பிட்டு ஒரு தோரயமாக்கப்பட்ட கட்டுபடுத்தப்பட்ட சோதனை.

தகவல் படிவம்

இந்த ஆய்வில் பங்கு கொள்வதற்க்கான அழைப்பு:

மன அழுத்தம் சம்பந்தமாக மருத்துவமனையில் அனுமதிக்கப்பட்டிருக்கும் நீங்கள் அதனுடைய அறிகுறிகளுக்கு GVV 278 மருந்து பயன்படுத்தலாமா என்று தெரிய இந்த ஆராய்ச்சியை பயன்படுத்துகின்றோம். மன நோயாளிகளுக்கு மன அழுத்தத்திற்க்கான புதிய மருந்தாகிய GVV278 உட்கொண்டு மன அழுத்தம் குறைந்து பயன் பெற அழைக்கின்றோம். இந்தாய்வில் இற்கிருந்து 30 பேரையும் இந்தியா உட்பட மற்ற நாடுகளில் 800 பேரை இவ்வாய்விற்கு மாதிரி எடுத்துக்காட்டாக இலக்கு வைத்துள்ளோம்.

இந்த ஆய்வை கிறிஸ்துவ மருத்துவ கல்லூரி வேலூர் மருத்துவ ஆய்வு குழு (ஆராய்ச்சி மற்றும் ஒழுங்குக்குழு) அங்கிகாரம் அளித்துள்ளது. ஆராய்ச்சியில் சேர்வதற்க்கு நோயாளிகள் மற்றும் அவர்களுடய உறவினர்களின் குணநலங்களை மதிப்பீடு செய்வதற்க்காக பண்ணுகின்ற ஆராய்ச்சியின் பாகமாக நடத்தப்படும் இந்த கற்பனை ஆராய்ச்சிக்கு அங்கீகாரம் பெறப்பட்டது.

இந்த புதிய மருந்து என்ன செய்யும்?

மன அழுத்தத்திற்க்கான புதிய மருந்தாகிய GVV278 யை மிருகங்களுக்கான ஆய்வுக்கூடத்தில் மிருகங்களுக்கு கொடுக்கப்பட்டு மிருகங்களின் மன அழுத்தம் குறைக்கப்பட்டதாக காண்பிக்கப்பட்டது. பின் விளைவுகளைக் குறித்து ஆராய்ச்சி செய்யப்பட்டது. மன நோயாளி இல்லாத 20 பேர் தெர்ந்தெடுத்து அவர்களுக்கு ஒரு வருடத்திற்கு GVV278 மருந்து 10mg, 20mg, 30mg போன்ற அளவுகளில் காலை சாப்பாட்டுக்குப் பிறகு உட்கொள்ளச் செய்து ஆராய்ச்சி செய்யப்பட்டது. இதன் மூலம் அறிந்துக் கொண்டது என்னவெனில் ஒரு நாளைக்கு 20mg உட்கொண்டவர்களுக்கு மன அழுத்தம் குறைவதற்க்கான அறிகுறிகள் தென்ப்பட்டது.

இன்னும் ஒர் ஆராய்ச்சியில் பிரேசில் நாட்டைச் சார்ந்த மனநோயாளிகள் 25 பேரை தெர்ந்தெடுத்து சிகிச்சையளிக்கப்பட்டது. அவர்களுக்கு சோர்வு தலைவலி தூக்கமின்மை எரிச்சல் போன்ற அறிகுறிகள் கொண்ட இவர்களுக்கு GVV278 கொடுக்கப்பட்டு மன அழுத்தம் போன்றவை குறைக்கப்பட்டது. இந்த ஆய்வு மிக குறைவான நோயாளிகளிடம் நடத்தப்பட்டது. ஏனென்றால் GVV278 ஒரு போலி மருந்தோடு ஒப்பிடப்படவில்லை. அதனால் அதிர்ஷ்டமாக வந்ததா அல்லது அவர்களின் வழக்கமான சிகிச்சையுடன் கூடுதலாக GVV 278 கொடுக்கப்பட்டு அதில் காணப்பட்ட முன்னேற்றமா என்று கண்டு பிடிக்க முடியவில்லை.

ஏற்கனவே உங்கள் மருத்துவர் பரிந்துரையின் அடிப்படையில் நீங்கள் மருந்து உட்கொண்டு வருகிறீர்கள் மற்ற மருந்துகளும் உங்கள் பிரச்சனைக்கு தீர்வு தரலாம்.

மன அழுத்தம் அறிகுறியுள்ளவர்களுக்கு இந்த GVV278 மருந்து எப்படி உதவுகிறது?

இந்த GVV278 மருந்துள்ள இரசாயன பொருள் மூளைக்கு சென்று ஒன்றாக வேலைச் செய்து விளைவுகளை ஏற்படுத்துகிறது என்பது தெரியாது. ஏனென்றால் மூளையில் பல்வேறு வேதியல் மாற்றங்கள் ஏற்படுவதால் குறிப்பிட்ட மாற்றங்களைப் பற்றி தெரியாது.

18. இவ்வாய்வு மருத்துவர் எப்படி செய்ய திட்டம் வைத்திருப்பார் அல்லது திட்டம் வைத்திருப்பதில் என்பதை பங்கு பெறும் நோயாளிகள் உதவி தேவையில்லை

    பலமாக ஒத்துக் கொள்கிறேன் /ஒத்துக் கொள்கிறேன் /தெரியாது /ஒத்துக் கொள்ளவில்லை /பலமாக ஒத்துக் கொள்ளவில்லை

19. புதிய மருந்து வேலை செய்வதினாலும் மருத்துவ ஆதாயம் பெற்றதினாலும் இதில் பங்குக் கொள்ள அழைப்பேன்

    பலமாக ஒத்துக் கொள்கிறேன் /ஒத்துக் கொள்கிறேன் /தெரியாது /ஒத்துக் கொள்ளவில்லை /பலமாக ஒத்துக் கொள்ளவில்லை

20. புதிய மருந்தும் மற்றும் அதே போல மற்றொரு மருந்தும் ஒப்பிட்டு பார்ப்பதற்கு இந்த ஆய்வில் பங்கு பெற எனக்கு அழைப்பு இருப்பின் சம்மதம் தெரிவிக்கின்றேன்.

    பலமாக ஒத்துக் கொள்கிறேன் /ஒத்துக் கொள்கிறேன் /தெரியாது /ஒத்துக் கொள்ளவில்லை /பலமாக ஒத்துக் கொள்ளவில்லை

11. இந்த மாதிரி ஆராய்ச்சிககு பங்கு பெறுதல் முக்கியமான துண்டுகோளாக நோயாளிகள் மருத்துவர் மீதும் மருத்துவமனை மீதும் நம்பிக்கை வைக்க வேண்டும்.

பலமாக ஒத்துக் கொள்கிறேன் /ஒத்துக் கொள்கிறேன் /தெரியாது /ஒத்துக் கொள்ளவில்லை /பலமாக ஒத்துக் கொள்ளவில்லை

12. உடன்பாடு படிவத்தில் உள்ளவற்றை புரிந்துக் கொள்ள நோயாளிக்கு சிரமமாக இருந்தது

பலமாக ஒத்துக் கொள்கிறேன் /ஒத்துக் கொள்கிறேன் /தெரியாது /ஒத்துக் கொள்ளவில்லை /பலமாக ஒத்துக் கொள்ளவில்லை

13. இவ்வாய்வில் பங்கு பெறுவது குறித்து குடும்பத்தினர் கூட முடிவு எடுப்பார்கள் இதில் தனிப்பட்ட முடிவில்லை

பலமாக ஒத்துக் கொள்கிறேன் /ஒத்துக் கொள்கிறேன் /தெரியாது /ஒத்துக் கொள்ளவில்லை /பலமாக ஒத்துக் கொள்ளவில்லை

14. பங்கு கொண்டதால் தான் மற்றவர்களுக்கு பாதுகாப்பான நம்பகமான விவரங்கள் தெரிய வரும்

பலமாக ஒத்துக் கொள்கிறேன் /ஒத்துக் கொள்கிறேன் /தெரியாது /ஒத்துக் கொள்ளவில்லை /பலமாக ஒத்துக் கொள்ளவில்லை

15. இந்த புது மருந்து அல்லது அதேப் போல இருக்கும் மருந்து யார் யாருக்கு கிடைக்கும் என்பதை நோயாளிகளோ மருத்துவரோ நியாயப்படுத்தப் முடியாது.

பலமாக ஒத்துக் கொள்கிறேன் /ஒத்துக் கொள்கிறேன் /தெரியாது /ஒத்துக் கொள்ளவில்லை /பலமாக ஒத்துக் கொள்ளவில்லை

16. (RCT's) இவ்வாய்வில் பங்கு பெறும் நோயாளிகள் பாதி பேருக்கு புதிய மருந்தைப் போல மற்றொரு மருந்து கொடுப்பது நல்லதல்ல என்று நியாயப்படுத்தப் முடியாது.

பலமாக ஒத்துக் கொள்கிறேன் /ஒத்துக் கொள்கிறேன் /தெரியாது /ஒத்துக் கொள்ளவில்லை /பலமாக ஒத்துக் கொள்ளவில்லை

17. உடன்பாடு பத்திரத்தின் மூலம் இவ்வாய்வில் பங்கு பெறும் நோயாளிகள் எங்கு எந்த மருத்துவர் எந்த மாதிரியான மருந்து என்பதை தெரிந்துக் உடன்பாடு பத்திரத்தில் கையெப்பமிடுவதில் நியாயபடுத்த முடியும்.

பலமாக ஒத்துக் கொள்கிறேன் /ஒத்துக் கொள்கிறேன் /தெரியாது /ஒத்துக் கொள்ளவில்லை /பலமாக ஒத்துக் கொள்ளவில்லை

// பக்கம் - 12 //

4. பண உதவி கிடைக்கும் என்று எதிர்பார்த்து இவ்வாய்வில் நோயாளிகள் பங்குக் கொள்கின்றனர்

பலமாக ஒத்துக் கொள்கிறேன் /ஒத்துக் கொள்கிறேன் /தெரியாது /ஒத்துக் கொள்ளவில்லை /பலமாக ஒத்துக் கொள்ளவில்லை

5. தன்னுடைய மருத்துவ தொழிலை பெருக்குவதற்கு மருத்துவர்கள் இவ்வாய்வை மேற்கொள்கின்றனர்

பலமாக ஒத்துக் கொள்கிறேன் /ஒத்துக் கொள்கிறேன் /தெரியாது /ஒத்துக் கொள்ளவில்லை /பலமாக ஒத்துக் கொள்ளவில்லை

6. இது போன்ற ஆய்வில் நோயாளிகள் பங்கு பெறுவது ஏனைன்றால் ஒட்டு மொத்த மனித துன்பத்தை குறைக்க உதவும் என நம்புகிறேன்

பலமாக ஒத்துக் கொள்கிறேன் /ஒத்துக் கொள்கிறேன் /தெரியாது /ஒத்துக் கொள்ளவில்லை /பலமாக ஒத்துக் கொள்ளவில்லை

7. இவ்வாய்வின் மூலம் மருத்துவரின் முக்கிய நோக்கமே நோயாளிக்கு உதவுவதேயாகும்

பலமாக ஒத்துக் கொள்கிறேன் /ஒத்துக் கொள்கிறேன் /தெரியாது /ஒத்துக் கொள்ளவில்லை /பலமாக ஒத்துக் கொள்ளவில்லை

8. ஆராய்ச்சி நடத்தும் மருத்துவமனை மற்றும் மருத்துவரின் நோக்கம் மேல் நம்பிக்கை நோயாளிகளுக்கு கடினம்

பலமாக ஒத்துக் கொள்கிறேன் /ஒத்துக் கொள்கிறேன் /தெரியாது /ஒத்துக் கொள்ளவில்லை /பலமாக ஒத்துக் கொள்ளவில்லை

9. இந்த ஆராய்ச்சியில் மருத்துவருக்கு அதிக நேரம் மற்றும் மற்ற நோயாளிகள் தலையிடு ஏற்பட வாய்ப்புண்டு

பலமாக ஒத்துக் கொள்கிறேன் /ஒத்துக் கொள்கிறேன் /தெரியாது /ஒத்துக் கொள்ளவில்லை /பலமாக ஒத்துக் கொள்ளவில்லை

10. புதிய மருந்தால் பாதுகாப்பு மற்றும் பயன்பட்டது போன்ற சந்தேகங்களுக்கு இந்த மாதியான ஆராய்ச்சியில் பத கிடைக்காது.

பலமாக ஒத்துக் கொள்கிறேன் /ஒத்துக் கொள்கிறேன் /தெரியாது /ஒத்துக் கொள்ளவில்லை /பலமாக ஒத்துக் கொள்ளவில்லை

Appendix 2

கேட்கப்படும் கேள்விகள் தங்களின் மதிப்பீடுகள்

கேள்விகளைப் பற்றிய தகவல்கள்: எந்த புதிய கண்டுபிடிப்பான மருந்துகள் உண்மையாக வேலை செய்கிறதா இல்லையா என்பதை கண்டறியும் முயையே RCT's என்று ஏற்கனவே உங்களுக்கு சொல்லப்பட்டது. புதிய மருந்தோ அல்லது அதேப் போலிருக்கும் மருந்து கொடுப்பதுப் பற்றி மருத்துவரோ அல்லது நோயாளியோ தீர்மானிக்க இயலாது. குலுக்கல் முறை போன்றே அமையும். சுாதாரணமாக நீங்கள் எதிர்ப்பார்ப்பதற்க்கும் மேலாக இது வித்தியாசமாக அமையும்.

இதில் பங்கு கொள்பவர்குளுக்கு வித்தியாசமான கருத்துகள் நம்பிக்கைகள் மற்றும் எண்ணங்கள் உடையவர்களாக இருப்பர். இந்த மாதரியான கருத்துக்கள் எண்ணங்கள் மற்றும் நம்பிக்கைகள் உடையவர்கள் இந்த ஆய்வில் பங்கு பெறலாமா வேண்டாமா என்பதை முடிவு பெற உதவிச் செய்யும். இதனாலேயே தனித்தனியாக கேள்விகள் கேட்கப்பட்டு உங்கள் கருத்துகளை குறித்துக் கொள்ளப்படும். இதில் நீங்கள் கூறும் பதில்கள் சரியா தவறா என்பது இல்லை. உங்கள் எண்ணங்கள் எங்கள் ஆராய்ச்சிக்கு மிக முக்கியம். ஒவ்வொன்றுக்கும் எதற்காக இதை ஏன் தெர்ந்தெடுத்தீர்கள் என்ற காரணத்தை சொல்லக் கேட்டு பதிலச் செய்து அதை நாங்கள்தெள்ளந்தெளிவாக புரிந்துக் கொள்வோம்.

சரியான பதில்களை வட்டமிடவும்:

1. புதிய மருந்துகளை மருத்துமனைகளில் கொடுக்கப்படுவத்தற்கு முன் அதை அறிவியல் பூர்வமாக சோதனை செய்யப்பட வேண்டும்?

   பலமாக ஒத்துக் கொள்கிறேன் /ஒத்துக் கொள்கிறேன் /தெரியாது /ஒத்துக் கொள்ளவில்லை /பலமாக ஒத்துக் கொள்ளவில்லை

2. ஆராய்ச்சியில் பங்குக் கொள்ளும் நோயாளிகள் இதில் பங்குக் பெறுவதால் தனி கவனமும் மற்றும் ஆரோக்கிய ஆதாயம் கிடைக்கும் என்று எதிர்பார்த்து பங்கு பெறுகிறார்கள்

   பலமாக ஒத்துக் கொள்கிறேன் /ஒத்துக் கொள்கிறேன் /தெரியாது /ஒத்துக் கொள்ளவில்லை /பலமாக ஒத்துக் கொள்ளவில்லை

3. ஆய்வு மருத்துவர்கள் நோயாளிகளின் மேல் இதை ஒரு பரிசோதனையாக செய்கிறார்கள்

   பலமாக ஒத்துக் கொள்கிறேன் /ஒத்துக் கொள்கிறேன் /தெரியாது /ஒத்துக் கொள்ளவில்லை /பலமாக ஒத்துக் கொள்ளவில்லை

என்னுடைய கருத்துக்கள் மற்றும் பதில்கள் பாதுகாக்கப்படும். வேறு யாருக்கும் வெளியிடப்பட மாட்டாது என்றும் ஆய்வின் முடிவுகளை மருத்துவ பத்திரிக்கையில் ஒட்டு மொத்த சிகிச்சையின் முடிவும் வெளியிடப்படும் என்றும புரிந்துக் கொண்டேன்.

இவ்வாய்வில் பங்கு கொள்வதால் என்னுடைய சிகிச்சைக்கு எந்த பாதிப்போ, எந்த நேரடி ஆதாயமோ, இழப்பீடோ கிடைக்காது என்பதை புரிந்துக் கொண்டேன்.

நான் பாதியில் விலகினாலும் இவ்வாய்க்குழு எப்போழுது வேண்டுமானாலும் என்னுடைய மருத்துவ பதிவை பார்க்க என்னுடைய அனுமதியோ / என்னுடைய உறவினர் அனுமதியோ தேவைப்படாது என்பதை புரிந்துக் கொண்டேன்.

இவ்வாய்விற்காய் டாக்டர்டோனோடுக்கும் பேட்டியில் பங்குக் கொள்ள நான் உடன்படுகிறேன்.

இவ்வாய்விற்காய்டாக்டர்சவ்மில் எடுக்கும் பேட்டியில் பங்குக் கொள்ள நான் உடன்படுகிறேன்.

பேட்டிகள் பதிவுச் செய்ய நான் உடன்படுகிறேன்.

பெயர்:

கையெப்பம்:

தேதி:

சாட்சியின் பெயர்:

பங்குபெறுபவரின் உறவுமுறை:

தேதி:

<u>உறவினரின் ஒப்புதல் படிவம்</u>

_____, ஆகிய நான் _____
உறவினருக்கு வாசித்து காண்பிக்கப்பட்டு சந்தேகங்கள் தீர்க்கப்பட்டு இதில் பங்குக் கொள்ள உடன்படுகிறேன்.

இந்த ஆய்வில் என்னுடைய பங்கு பெறுதல் மற்றும் இந்த தகவல் படிவத்தில் உள்ள விதிகள் எடுத்துரைக்கப்பட்டது.

பெயர்:

~~கையெப்பம்~~: கையொப்பம் ;

தேதி:

பங்குபெறுபவரின் உறவுமுறை:

// பக்கம் - 9//

அறிவிக்கப்பட்ட உடன்பாடு பத்திரம்

ஆராய்ச்சியின் தலைப்பு: சுழற்சி முறையில் நடத்தப்படும் ஆராய்ச்சியில் பங்குபெறுபவரின் மனோபாவத்தை மதிப்பிடுதல் மனமுவந்து பங்கேற்க விருப்பும் தயீதலீ மற்றும் பங்கு கொள்ளும் திறமை ஆகியவைகளை அளவிடுதல்.

ஆராய்ச்சி செய்பவர்கள் மற்றும் கல்வி நிறுவனம் பற்றிய தகவல்: டாக்டர் டோனே ஜார்ஜ், டாக்டர் சவ்மில் டோலக்கியா, டாக்டர் பிரதாப் தரியன் - கிறிஸ்துவ மருத்துவக் கல்லூரி வேலூர்.

படிப்பு எண்:

பங்கு பெறுபவரின் பெயர்:

பிறந்த தேதி / வயது (வருடங்களில்):

நிலைமை: உள்நோயாளி / உள்நோயாளியின் உறவினர்

_____, ஆகிய நான் _____ மகன் / மகள் _____ கொடுக்கப்பட்ட அறிவிப்பு தாளிலிருந்து வாசித்து / வாசித்துக் காண்பிக்கப்பட்டு இது சமபந்தமாக இருந்த சந்தேகங்களை தெளிவிக்கப்பட்டது.

இதில் நான் மனமுவந்து பங்கு கொள்ளுதலும் எப்போழுது வேண்டுமானலும் விலகிக் கொள்வதாலும் இதனால் என்னுடைய சிகிச்சைக்கோ என் உறவினருடைய சிகிச்சைக்கோ எந்த பாதிப்பும் இல்லாமல் கிடைக்கும் மருத்துவம் தடைபடாது மற்றும் இது என்னுடைய உரிமை மற்றும் எங்கள் உரிமை என்பதை புரிந்துக் கொண்டேன்.

இந்தப் புதிய மருத்துவ ஆராய்ச்சி பற்றிய என் கருத்துகளை கேட்டு ஆய்வில் ஒரு பகுதியாக எடுத்து விவாதிக்க மருத்துவர் டோனே ஜார்ஜ் நடத்தும் நேர்காணலில் கலந்துக் கொள்ள வேண்டும் என்றும் அரை மணி நேரத்திலிருந்து ஒரு மணி நேரமாகவோ அல்லது அதற்கும் மேலாக நீடிக்கும் என்று புரிந்துக் கொண்டேன்.

ஒரு பேட்டி முடிந்தப்பின்பு டாக்டர் சவ்மில்அவர்களால் மற்றொரு அரை மணி நேரப் பேட்டியில் பங்குக் கொண்டு எந்த அளவு புரிந்து கொண்டேன் என்பதை அறியவே எடுக்கப்படுகிறது.

பேட்டிகளில் கேட்கப்படும் கேள்விகளுக்கு என்னால் ஆன பதில்களையும் ஒத்துழைப்பையும் அளிக்க வேண்டும் என்பதை புரிந்துக் கொண்டேன்.

பேட்டி நடக்கும் போது ஒலி நாடாவில் பதிவுச் செய்து தவறிய கருத்துக்களை போட்டுக் கேட்டு சரி செய்யப்படும். இது இன்னாருடைய குரல் என்று யாராலும் கண்டு பிடிக்கமாட்டாது என்று உணர்ந்துக் கொண்டேன்.

// பக்கம் - 8 //

கேள்விகள் மற்றும் சந்தேகங்கள் இருப்பின் யாரை தொடர்புக் கொள்வது?

டாக்டர் டோனே ஜார்ஜ், 0416 228 4485 டாக்டர் சவ்மில் டோலக்கியா, டாக்டர் பிரதாப் தரியன் - 0416-2284520 கிறிஸ்துவ மருத்துவக் கல்லூரி மனோத்துவ துறை யூனிட் - 2 அலுவலகத்திலும் தொடர்புக் கொள்ளலாம்.

// பக்கம் - 7 //

இவ்வாய்வில் பங்கு கொள்ள நீங்கள் சம்மதித்தால் உங்களுடைய பொறுப்புகள் என்ன?

நீங்கள் பங்கு கொள்ள சம்மதித்தால் எல்லா பேட்டியிலும் கலந்து கொண்டு கேட்கப்படும் கேள்விகளுக்கு உங்கள் பதில்களையும் கருத்துகளும் மட்டுமே எதிர்பார்கின்றோம். வேறு எந்த பொறுப்புகளும் உங்களிடமிருந்து எதிர்ப்பார்க்கப்பட்டது.

பெறப்படும் தகவல்கள் ரகசியமாக வைக்கப்படுமா?

ஆம். பெறப்படும் தகவல்களும் கருத்துகளும் நிச்சயமாக பாதுகாப்பாக வைக்கப்படும். உங்களை பேட்டியை எடுத்தவருக்கு மட்டுமே உங்களையும் உங்கள் பெயர் உங்கள் குரல் மட்டும் தெரியும் மற்றும் பதிவு செய்த உங்கள் குரலுக்கு பதிவு எண் வழங்கப்படும். வேறு யாராலும் அதை கண்டு பிடிக்க இயலாது.

இந்த ஆராய்ச்சியில் பங்கு கொள்வதால் என்ன பயன்?

நாங்கள் இந்த மருத்துவமனையில் வழங்கும் சிகிச்சையில் மாற்றம் செய்வதோ அல்லது சேர்ப்பதோ இல்லை. இந்த ஆய்வில் பங்கு பெறுவதால் நீங்கள் நேரடியாக பயன் பெற முடியாது. மற்றும் நீங்கள் இதன் மூலம் பணம் அல்லது மற்ற இழப்பீடு வழங்கப்பட மாட்டாது. எனினும் இந்த ஆய்வின் மூலம் புதிய மருந்துப் பற்றிய ஆய்வை அறிந்துக் கொள்ள உதவும். எனவே இந்த ஆய்வில் நீங்கள் பங்கேற்பதன் மூலம் இந்தப் புதிய மருந்து பற்றிய ஆய்வில் எதிர்க்காலத்தில் மற்ற நோயாளிகளுக்கு உதவும்.

இந்த ஆராய்ச்சியில் பங்கு கொள்வதால் ஆபத்து ஏற்படுமா?

இந்தராய்ச்சியில் பங்கு கொள்வதால் ஆபத்து ஏதுமில்லை கேட்கப்படும் கேள்விகள் உங்களுக்கு வருத்தம் கஷ்டம் தருவதாக இருந்தால் அதற்கு பதில் அளிக்க வேண்டாம். களைப்பாகவோ கஷ்டமாகவோ இருந்தால் பேட்டியை நிறுத்தி பின்னர் தொடரப்படும்.

இவ்வாய்வில் பங்கு கொண்டப்பின் திரும்பப் பெறலாமா அல்லது விலகிக் கொள்ளலாமா?

இவ்வாய்வில் பங்கு கொள்ள ஒப்புக் கொண்டப் பிறகு உங்களுக்கு தொடர்ந்து கலந்து கொள்ள உடன்பாடு / சம்மதம் இல்லையெனில் நீங்கள் விலகிக் கொள்ளலாம். ஆனால் பாதியில் விலகுவதற்க்கும் தேவையான சரியான காரணங்கள் எதிர்பார்க்கின்றோம்.

நீங்கள் இவ்வாய்விலிருந்து விலகிக் கொள்வதால் நாங்கள் அதிருப்தியோ அல்லது வருத்தமோ அடைய மாட்டோம். மேலும் இவ்வாய்வில் பங்கு பெறுவதோ அல்லது பெறாமல் இருப்பதோ இந்த மருத்துவமனையில் சிகிச்சையை பாதிக்காது.

இவ்வாய்விற்கு யார் பணம் செலவிடுகிறார்கள்?

தனிப்பட்ட முறையில் இவ்வாய்விற்கு பணம் செலவிடுவதில்லை. பேட்டியின் கேள்வித்தாளுக்கும் மொழியாக்கத்திற்க்கும் தங்கள் கருத்துகளை பதிவு செய்வதற்க்கும் முடிவுகளை ஆராய்வதற்கும் வேலூரில் உள்ள சி.எம்.சி ஆராய்ச்சிகளுக்கு என்று ஒதுக்கப்பட்ட பணத்திலிருந்து செலவிடப்படுகின்றது.

இவ்வாய்வின் முடிவுகளை நான் அறிந்துக் கொள்ளலாமா?

ஆய்வின் முடிவுகளை மருத்துவ பத்திரிக்கையில் ஒட்டு மொத்த சிகிச்சையின் முடிவும் வெளியிடப்படும். தனி நபரின் சிகிச்சையின் முடிவு வெளியிடப்படமாட்டாது. இதனால் இன்னாரின் சிகிச்சையின் முடிவு என்று யாராலும் கண்டுபிடிக்கப்பட மாட்டாது. ஆய்வின் முடிவுகளை அறிய விரும்பினால் உங்கள் முகவரி கிடைக்கும் பட்சத்தில் இந்த மருத்துவ பத்திரிக்கை அனுப்பி வைக்கப்படும்.

தகவல் தாள் முதல் பகுதியில் உள்ள கேள்விகளை வாசித்துக் காட்டி அதன் பிறகு நீங்கள் புரிந்து கொண்ட பதிலை அறிய விரும்புகிறோம். இது பரீட்சையோ ஞாபகசக்திக்கு ஓர் சோதனையோ அல்லது எவ்வளவு புரிந்துக் கொண்டீர்கள் என்று அறியவோ அல்ல உங்கள் கருத்துக்களை அறியவே முயற்சி செய்கின்றோம்.

இதைப் போல ஒரு தகவல் மாதிரி படிவத்தை உங்களிடம் வாசித்துக் காட்டுவேன். இந்த தகவல் படிவம் கற்பனை ஆய்வில் பங்கு கொள்ள ஓர் அழைப்பு. இந்த கற்பனை ஆய்வில் பங்கு கொள்ளலாம் என்பவர்களுக்கு புதிய மருந்தோ அல்லது அதைப் போல ஒரு மருந்து கொடுக்கப்படும். இந்த ஆய்வில் பங்கு கொள்வது யார்? எப்படி பங்கு கொள்ள முடியும்? என்பதைப் பற்றியும் எடுத்துரைத்து இந்த பரிசோதனை ஆய்விற்கு உங்களை அழைக்கின்றோம். என்னவென்றால் இந்த அழைப்பிதழ் உண்மையானதல்ல ஏனென்றால் நீங்கள் இந்த ஆய்வில் பங்கேற்பீர்களா என்பதற்க்கான சோதனை (அல்லது) அனுமதிப்பீர்களா என்று எதிர்பார்த்தோம். ஆனால் நீங்கள் இந்தச் சோதனை பற்றி அறிந்துக் கொள்வதற்க்கான ஒரு பயிற்சி ஆகும். நீங்கள் இந்த அழைப்பின் மூலம் இச்சோதனை பற்றி என்ன நினைக்கிறீர்கள்? இது ஒரு கற்பனை ஆய்வேயாகும். இதே போல் இருக்கும் மற்ற ஆய்வின் மாதிரியேயாகும். இதன் மூலம் உங்கள் கருத்துக்கள் புரிந்துக் கொண்டு செயல்ப்பட உதவியாக இருக்கும்.

நீங்கள் கேள்விகள் கேட்க தருணம் அளிக்கப்படும். இதன் மூலம் நீங்கள் எவ்வளவு தூரம் புரிந்துக்கொண்டீர்கள் என்பதை நாங்கள் அறிந்து கொள்வோம்.

சிகிச்சை பெறுபவராக இருக்கும் நீங்கள் பங்கு பெற முடிவு செய்வதற்கு எது உதவியது என்றும் நோயாளியின் உறவினராக இருந்தால் இந்தராய்ச்சியில் பங்கு பெற முடிவு செய்வதற்கு முக்கிய காரணம் என்னசென்றும் தெரிந்துக் கொள்ள ஆவலாக உள்ளோம்.

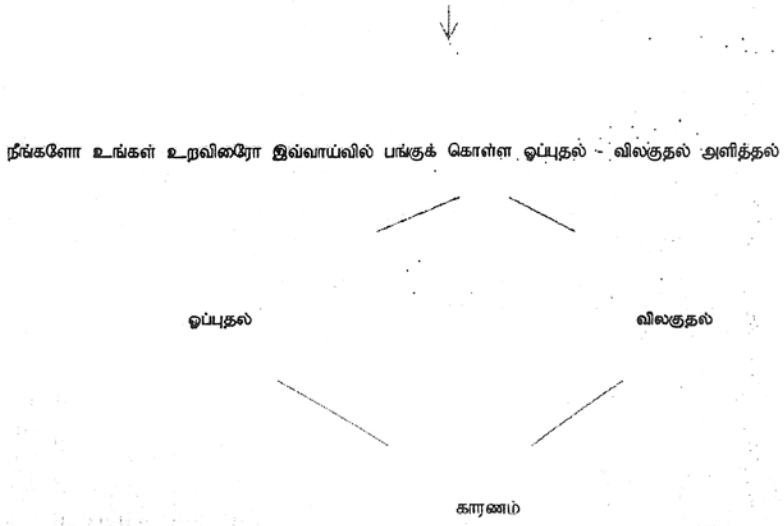
சிகிச்சை பெறுபவராக இருக்கும் நீங்கள் உங்களுக்கு விருப்பமில்லையானால் ஏன் விருப்பமில்லை என்பதை அறிய ஆவலாக உள்ளோம். நோயாளியின் உறவினராக இருக்கும் நீங்கள் உங்கள் உறவிரை பங்கு பெற விருப்பமில்லையானால் ஏன் என்பதையும் அறிய ஆவலாக உள்ளோம்.

சிகிச்சை பெறுபவராக (நோயாளியாக) இருக்கும் நீங்கள் பங்கு பெற முடிவு செய்தப்பின் அதோடு கூட விரிவுபடுத்தப்பட்ட மற்றொரு ஆராய்ச்சியாக ரத்த பரிசோதனைக்கும் மற்றும் சில பரிசோதனைக்கும் உட்பட வேண்டியுள்ளது. இந்த ஆய்வை பற்றி எடுத்துரைக்கப்படும். குறித்து வைக்கப்படும். இதில் பங்கு கொள்ள அனுமதி அளித்தால் குறித்து வைக்கப்படும். சிகிச்சை பெறுபவரின் (நோயாளியாக) இருக்கும் நீங்கள் உங்கள் கருத்துகளையும் மற்றும் பங்குக் கொள்ளவோ அல்லது மறுப்பு தெரிவித்தாலோ மறுப்பிற்க்குரிய காரணத்துடன் குறித்து வைக்கப்படும். இவ்வராய்ச்சியில் கலந்து கொள்ள சம்மதம் / சம்மதமில்லை என்றால் பேட்டி அத்துடன் முடிவடைகிறது.

இந்த ஆராய்ச்சியில் எனது மூத்த அதிகாரியும் இதே மருத்துவமனையில் பணிபுரியும் டாக்டர் சல்மில் டோலக்கியா அவர்கள் உங்களை சில கேள்விகள் கேட்டு அதன் மூலம் நீங்கள் எவ்வளவு புரிந்துள்ளீர்கள் என்பதை அறிய உங்கள் ஒத்துழைப்பு தேவை. அவருடைய இந்த பேட்டியான என்னுடைய பேட்டியைத் தொடர்ந்து 24 – 48 மணி நேரத்திற்க்குள்ளாக நடைபெறும். அரை மணி நேரம் இந்த பேட்டி நடைபெறும்.

சேகரிக்கப்படும் உங்கள் கருத்துக்கள் தகவல்கள் அனைனத்தும் பதிவு செய்யப்பட்டு எவ்வளவு தூரம் புரிந்து வைத்துள்ளீர்கள் மற்றும் உங்களுடைய தீர்மானம் எல்லாவற்றுக்கும் பொருந்தி வருகிறதா என்பதையும் அறிய உதவும். மேலும் இந்த ஆராய்ச்சியில் பங்கு கொள்ளும் ஒவ்வொருவருடனும் இந்த கேள்விகள் கேட்கலாமா என்று தீர்மானிக்கப்படும்.

விரிவான ஆராய்ச்சிக்கு அழைப்பு. விரிவான ஆராங்ச்சியைப் பற்றிய தகவல்களை புரிந்துக் கொள்ளுதல்



இவ்வாய்வில் பங்கு பெற விரும்பினால் "இதில் பங்கு கொள்வது என் சொந்த விருப்பமே யாருடைய வற்புறுத்தலும் இல்லை" என்று எழதப்பட்டிருக்கும் பாரத்தில் கையெப்பமிட வேண்டும். இதன் மூலம் நீங்கள் இவ்வாய்வில் பங்கு கொள்ள விருப்பம் தெரிவித்து உள்ளீர்கள் தங்கள் விருப்பமின்றி மருத்துவர் ஏதுவும் செய்ய மாட்டார் என அறிவதற்கே இந்த கையெழுத்து வாங்கப்படுகிறது. இவ்வாய்விலிருந்து . எப்போது வேண்டுமானாலும் விலகிக் கொள்ளலாம்.

உங்களை ஒரு தனிப்பட்ட இடத்தில் வைத்து கேள்விகள் கேட்கப்படும்இந்த பேட்டி குறைந்தது ஒரு மணி நேரம் நீடிக்கும். கேள்விகள் புரிந்து கொள்வதற்கேற்ப (அதாவது சுலபமாகவோ – கடினமாகவோ கொஞ்சம் நேரமோ அல்லது அதிக நேரமோ ஆகலாம்.

பேட்டி நடக்கும் போது நீங்கள் சொல்லும் கருத்துகளில் சிலவற்றை தவற வாய்ப்பிருக்கிறது. ஆகலால் நீங்கள் சொல்வதை ஒலி நாடாவில் பதிவுச் செய்ய அனுமதி கொடுங்கள். டாக்டர் பிரதாப் தரியன் , என்னுடைய மேற்பாவையாளர் இந்த பேட்டியை ஒலிநாடாவில் கேட்டு நான தவறு ஏதெனும் செய்தால் திருத்தப்படும். பதிவு செய்த பேட்டியிலிருந்து பொதுவான கருத்துகளை புரிந்து கொள்வதுடன் இவ்வராய்ச்சியை மேலும் செம்மைபடுத்த உதவும். இது இன்னாருடைய குரல் என்று யாராலும் கண்டு பிடிக்கமாட்டாது. உங்களுடைய குரலுக்கு ஒரு ரகசிய எண் வழங்கப்படும்.

நீங்கள் சிகிச்சை பெறும் நோயாளியாக இருந்தால் உங்களுடைய விவரம் மனோத்துவ நிலை மற்றும் சிகிச்சை முறை பற்றிய கேள்விகள் கேட்கப்படும். நீங்கள் சிகிச்சை பெறுபவரின் உறவினராக இருந்தால் உங்களுடைய விவரம் சிகிச்சை பெறுபவருக்கும் உள்ள உறவு முறை பற்றி கேள்விகள் கேட்கப்பட்டு நீங்கள் சொல்லும் குறிப்பு எடுக்கப்படும்.

// பக்கம் - 4 //

பங்கு பெறுவதற்கு ஒப்பதல்

தகவல் படிவத்தில் கையெப்பமிடல்

விவரங்களை எடுத்துரைத்தப் பிறகு மனமுவந்து ஒப்புதல்

எப்போது வேண்டுமானாலும் விலகிக் கொள்ளலாம்.

பேட்டி ஒரு மணி நேரம் ஆகும்

நோயாளி மற்றும்
உறவினர்களிடம்
தனியான பேட்டி

களைப்பாக இருக்கும் போது
பேட்டியை நிறுத்தி பின்னர்
தொடரப்படும்

ஒலிநாடாவில் பதிவு
செய்ய அனுமதி

உங்களைப் பற்றியும்
உங்கள் நிலையைப்
பற்றியும்

இந்த ஆராய்ச்சியைப் பற்றி கேட்க்கப்படும் உங்கள் கருத்துக்கள்

பகுதி – 2

கற்பனை ஆய்வில் பங்குக் கொள்ள அழைப்பு

கற்பனை ஆய்விற்க்கான தகவல்களை தகவல் படிவத்திலிருந்து படித்து தெரிந்துக் கொள்ளுதல்

ஆய்வைக்குறித்த சந்தேகங்களை தெளிவாக்கப்பட்டது

நீங்களோ உங்கள் உறவினரோ இவ்வாய்வில் பங்குக் கொள்ள ஒப்புதல் - விலகுதல் அளித்தல்

ஒப்புதல்

விலகுதல்

இந்த முடிவு எடுக்க காரணம்

புதிய மருந்து அதிக பயனளிக்கக் கூடியதாகவோ குறைந்த பயனளிக்கக் கூடியதாகவோ மாற்றம் இல்லாததாகவோ இருப்பதற்கான காரணம் மருத்துவர்கள் நோயாளிகளை ஆராய்ச்சிக்கு நேர்ந்தெடுத்த விதமாகும். ஆராய்ச்சியின் துவக்கத்தில் புதிய மருந்து தேர்ந்தெடுக்கப்பட்ட நபர்களின் நோயின் தன்மை மற்றவர்களை விட அதிகமாகவோ குறைவாகவோ உடையவராகவோ இருக்கலாம். இதனால் ஆராய்ச்சியின் முடிவில் பாதிப்பு ஏற்படலாம். இந்த மாற்றங்கள் புதிய மருந்தினால் உண்டானவை என்பதை உறுதி செய்வது மிக முக்கியம். நோயாளிகளை முறைப்படி தேர்ந்தெடுக்க நோயாளிகளை லாட்டரி முறையிலோ அல்லது நாணயத்தை சுழற்றி பார்ப்பது முறையில் செய்யப்படும். இவ்வாறு செய்வது ஆராய்ச்சியில் பங்கெடுக்க அனைவருக்கும் புதிய மருந்து கிடைக்க சம வாய்ப்பு கிடைப்பதை உறுதி செய்யலாம்.

இந்த ஆராய்ச்சியின் முழுமையான தன்மையை புரிந்துக் கொண்டால் இதில் பங்கேற்க பலரும் முன் வருவர். இவ்வராய்ச்சியின் கடினமான காரியம் என்னவெனில் மக்கள் ஒருவரிலிருந்து மற்றவர்கள் வேறுபட்டவர்கள் பங்கு பெற விருப்பமில்லாதிருத்தல் தெளிவாக விளக்கப்பட்டாலும் புரிந்துக் கொள்ள முடியாத நிலைமை மற்றும் அநேக முறை விளக்கிக் கூறினாலும் திருப்தியற்ற பதில் தருவது போன்றவையாகும். அதிக வாய்ப்புகளும் மற்றும் ஆராய்ச்சியாளர்கள் பங்கு பெறுபவர்களின் கஷ்டங்களை புரிந்துக் கொண்டு செயல்படுவதிளாலும் ஆராய்ச்சியில் நோயாளிகள் உதவி செய்கின்ற மாதிரி திட்டம் செய்வதினால் அதிக வாய்ப்பு. இதன் மூலம் மருத்துவர் எந்த தீர்மானம் அல்லது முடிவும் செய்ய முடியாது மற்றும் நோயாளி அவன் (அல்லது) அவள் புதிய மருந்து வாங்குவதோ, பெறுவதோ (அல்லது) தேர்வு செய்யவோ முடியாது.

எனினும் மருந்துவர்கள் இந்த ஆய்வில் புதிய மருந்து பெற்றவர்கள் மற்றம் பெறாதவர்கள் யார் என்பதை கண்டறிந்து அதில் புதிய மருந்து உட்கொண்டவருக்கு ஏற்படும் சாதகமான விளைவுகள் ஏற்படுகிறதா (அல்லது) பக்க விளைவுகள் உருவாக்கி உள்ளதா என்று பார்க்க முடியும். இது நடைபெறுவதை தவிர்ப்பதற்க்காக புது மருந்து கிடைக்காதவர்களுக்கு வெற்று மாத்திரையை பெறுவார்கள. அதில் உள்ள மருந்து கெட்ட விளைவுகளை ஏற்படுத்ததாது. வெற்று மாத்திரை எல்லா விதத்திலும் புதிய மாத்திரையைப் போல உள்ளதால் நோயாளிகளுக்கும் மருத்துவர்களுக்கும் யார் எந்த மாத்திரையை எடுக்கிறார்கள் என்று தெரியாது.

இந்த ஆராய்ச்சியில் புது மருந்து கொடுப்பது பற்றி கருத்துகளை கேட்டு புரிந்துக் கொண்டு வருங்காலத்தில் பரிசோதனைகள் மேம்பட உதவிச் செய்ய மிகவும் பயன் உள்ளதாக இருக்கும். நான் செய்யும் ஆய்வில் மருந்து கொடுப்பது என்னுடைய நோக்கம் அல்ல.

<u>பங்கு பெற விருப்பம் உள்ளவர்கள் செய்ய வேண்டியது என்ன?</u> இவ்வாய்வில் 3 பகுதிகள் உள்ளன. முதல் 2 பகுதிகள் என்னாலும் மூன்றாம் பகுதி என்னுடன் பணியாற்றும் டாக்டர் டோலக்கியா அவர்களுடன் நடத்தப்படும்.

தகவல் படிவம்

ஆராய்ச்சியின் தலைப்பு: சுழற்சி முறையில் நடத்தப்படும் ஆராய்ச்சியில் பங்குபெறுபவரின் மனோபாவத்தை மதிப்பிடுதல் மனமுவந்து பங்கேற்க விருப்பம் தருதல் மற்றும் பங்கு கொள்ளும் திறமை ஆகியவைகளை ஆளவிடுதல்.

ஆராய்ச்சி செய்பவர்கள் மற்றும் கல்வி நிறுவனம் பற்றிய தகவல்:

டாக்டர் டோனே ஜார்ஜ், டாக்டர் சவ்மில் டோலக்கியா, டாக்டர் பிரதாப் தரியன் கிறிஸ்துவ மருத்துவக் கல்லூரி வேலூர்.

ஆராய்ச்சிக்கு அழைப்பு: என் பெயர் டாக்டர் டோனே ஜார்ஜ், நான் இந்த மருத்துவமனையில் மனோதத்துவ மேற்படிப்பு படிக்கின்றேன். நான் மேற்க்கொள்ளும் ஆராய்ச்சியில் உங்களின் உதவி தேவைப்படுகிறது. இந்த ஆராய்ச்சியில் பங்கு கொள்ளவும் இதைப் பற்றிய தகவல் பெறவும் உங்களை அழைக்கின்றேன்.

இந்த தகவல்படிவம் மூலம் இவ்வராய்ச்சிப் பற்றி விரிவாக எடுத்துரைக்கிறது. நீங்கள் பங்கு கொள்ள முடிவு எடுக்கும் முன் இப்படிவத்தில் எதாவது கேள்விகள் இருக்குமாயின் பதில் அளித்து விரிவாக விளக்கம் அளிக்கப்படும். நீங்கள் பங்கு கொள்வது இந்த மருத்துவமனையில் அளிக்கப்படும் சிகிச்சையின் ஒரு பங்கும் இல்லை. இவ்வராய்ச்சியில் பங்கு பெறவோ பெறாமல் இருப்பதோ இந்த மருத்துவமனையில் அளிக்கப்படும் சிகிச்சையை பாதிக்காது.

உங்களுக்கு சிகிச்சை அளிக்கும் மருத்துவர்களுக்கு இவ்வராய்ச்சிப் பற்றி தெரியும். இந்த மருத்துவமனையில் பணி செய்யும் மருத்துவ ஆலோசகராக டாக்டர் சவ்மில் டோலக்கியா எனக்கு இவ்வராய்ச்சியில் உதவி செய்கிறார் மற்றும், டாக்டர் பிரதாப் தரியன் என்ற மனோதத்துவ பேராசிரியர் என் வேலையை மேற்பார்வையிடுகிறார்.

ஆராய்ச்சியின் நோக்கம்: மனோரீதியான பிரச்சினையின் காரணமாக இம்மருத்துவமனையில் அனுமதிக்கப்பட்டுள்ள 30 பேரையும் அவர்களோடு இருக்கும் ஒர் உறவிரையும் பேட்டி காண்பது இவ்வராய்ச்சியின் நோக்கம். மேலும் மனோத்துவ பிரச்சனைகளுக்கு அளிக்க புதிய மருந்துகளை கண்டுபிடிப்பதைப் பற்றி மனப் பிரச்சினை உள்ளவர்களும் மற்றும் அவர்கள் குடும்பத்தினருடைய எண்ணத்தையும் புரிந்துக் கொள்வது இவ்வராய்ச்சியின் நோக்கம்.

புதிய மருந்துகளை படிப்பதில் எவ்வகையான ஆராய்ச்சி பயன்படுகிறது: மனப்பிரச்சினை உள்ளவர்களுக்கு அளிக்கப்படும் அந்த புதிய மருந்தும் அரசால் அங்கீகரிக்கப்பட முதலில் இவ்வகை பிரச்சினை உள்ள நபருக்கு அளித்து பார்க்கப்பட வேண்டும். ஆராய்ச்சிக் கூடத்தில் பரிசோதனைக்குப் பிறகு சிலரிடம் எந்த மருந்தை எந்த அளவு கொடுக்க வேண்டும் என்றும் அது பாதுகாப்பானதா என்றும் பார்க்கப்பட வேண்டும். இவ்வாறு செய்தப் பிறகு பலரிடம் இது பயன்படுத்தப்பட்டு இவர்களுடன் மருந்து சாப்பிடாத பலருடனும் ஒப்பிட்டு பார்க்கப்படுகின்றது. இப்புதிய மருந்தை உட்கொள்ளும் நபர்களிடம் ஏதாவது முன்னேற்றமோ அல்லது பிரச்சினையோ காணப்பட்டால் அது இம்மருந்தினால் தான் நிகழ்ந்தது அது தன்னிச்கையாகவோ வேறு காரணங்களினால் அல்ல என்பது அறிந்து கொள்ள இதுவே ஒரே வழி.